# DISCOVERY OF NEW ANTI-CRYPTOSPORIDIAL STRUCTURES FROM NATURAL PRODUCTS AND POTENTIAL SYNERGISTIC ANTI-CRYPTOSPORIDIAL ACTIVITY BY DRUG COMBINATIONS

A Dissertation

by

ZI JIN

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| Chair of Committee, | Guan Zhu |
| Committee Members, | Angela Arenas |
| | James J. Cai |
| | Yanan Tian |
| Head of Department, | Ramesh Vemulapalli |

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# ABSTRACT

*Cryptosporidium parvum* is a zoonotic parasitic protist and the causative agent of cryptosporidiosis in humans and animals. The main symptom of cryptosporidiosis is diarrhea, which can be severe and life-threatening in immunocompromised patients and young animals. However, current therapeutics are limited. In humans, nitazoxanide (NTZ) is the only FDA-approved treatment for immunocompetent patients. In animals, only halofuginone lactate (Halocur) is approved in a few countries for veterinary use in calves and lambs. Additionally, both NTZ and Halocur are not 100% effective against cryptosporidiosis. Therefore, there is an urgent demand for developing more effective chemotherapies.

The ultimate goal of this study is to discover potential new anti-cryptosporidial therapeutic options. Towards achieving this goal, we conducted phenotypic screening to identify new anti-cryptosporidial structures from 800 natural products and to explore combination of drugs with different targets for potential anti-cryptosporidial synergistic effect. Both approaches employed an in vitro model of infection by *C. parvum*. For natural products screening, we have identified 16 top hits with anti-cryptosporidia efficacies ($EC_{50}$ values from 0.122 to 3.940 μM) and cytotoxicity to host cell ($TC_{50}$ values from 6.31 to >100 μM), showing low to sub-micromolar anti-parasitic activity in vitro. Among them, three compounds with sub-micromolar $EC_{50}$ values (i.e., cedrelone, deoxysappanone B 7,4'-dimethyl ether [Deox B 7,4] and baicalein) were further investigated for their effectiveness on various parasite developmental stages in vitro. Cedrelone [CAS # 1254-85-9] and baicalein [CAS # 491-67-8] were more effective than Dexo B 7,4 [674786-37-9] when treating parasite for shorter periods of time, but all three compounds could kill the parasite irreversibly. For drug combination study of 9 pairs using 6

drugs, preliminary data indicated that the “paromomycin + vatalanib”, “paromomycin + vorinostat” and “paromomycin + triacsin C” produced synergistic effect. These observations pointed out a new direction to potentially synergize the anti-cryptosporidial efficacy and/or reduce the adverse effects of drugs at therapeutic doses.

In summary, we have discovered a set of new structures from natural products with excellent anti-cryptosporidial efficacies in vitro for future drug design and development, and identified new options in combination therapy against cryptosporidiosis in humans and animals.

# DEDICATION

To my beloved Father, Daxing Jin, he has been teaching me the importance of being brave to step out of my comfort zone and to enjoy each moment I experienced. Throughout my entire graduate career, without his endless support and encouragement, it is hard to imagine that I can complete my research and graduate as a Ph.D.

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## Contributors

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# NOMENCLATURE

| | |
|---|---|
| ACS | Acyl-CoA Synthetase |
| AIDS | Acquired Immunodeficiency Syndrome |
| Caco-2 | Human Colonic Adenocarcinoma Cells |
| CDC | Centers for Disease Control and Prevention |
| CDPK | Calcium Dependent Protein Kinase |
| $C_T$ | Cycle Threshold |
| Deox B 7,3 | Deoxysappanone B 7,3'-Dimethyl Ether Acetate |
| Deox B 7,4 | Deoxysappanone B 7,4'-Dimethyl Ether |
| DMSO | Dimethyl Sulfoxide |
| FBS | Fetal Bovine Serum |
| FDA | Food and Drug Administration |
| HCT-8 | Human Colonic Tumor 8 Cells |
| HDAC | Histone-Deacetylase |
| HIV | Human Immunodeficiency Virus |
| HPI | Hours Post Infection Time |
| HTS | High-Throughput Screening |
| IMPDH | Inosine-5’-mono-phosphate Dehydrogenase |
| NIH | National Institutes of Health |
| NTZ | Nitazoxanide |
| PBS | Phosphate-Buffered Saline |
| PCR | Polymerase Chain Reaction |

| | |
|---|---|
| PI(4)K | Phosphatidylinositol-4-OH Kinase |
| PRM | Paromomycin |
| PVM | Parasitophorous Vacuole Membrane |
| PVS | Phenyl Vinyl Sulfone |
| qRT-PCR | Quantitative Reverse Transcriptase-Polymerase Chain Reaction |
| SAR | Structure-Activity Relationship |
| SI | Safety Interval |
| TC | Cytotoxicity |
| UV | Ultraviolet |
| 2DG | 2-deoxyglucose |

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# CHAPTER I

# INTRODUCTION

## 1.1. History of *Cryptosporidium* spp.

*Cryptosporidium* is a genus of parasitic protist in the Phylum Apicomplexa (which includes *Plasmodium, Toxoplasma* and *Babesia*) of both medical and veterinary importance. *Cryptosporidium muris* (*C. muris*) was the first species detected and named by Dr. Ernest E. Tyzzer from the mouse gastrointestinal tract in 1907 [1]. He precisely described its morphology and life cycle and placed it in the coccidian family due to the absence of sporocysts in the oocysts. Later, in 1912, *Cryptosporidium parvum* (*C. parvum*) was isolated from small intestinal and considered as new species due the production of smaller sized oocysts [2]. People have neglected *C. parvum* for more than half century since its first discovery. Only a few of researchers, medical practitioners and veterinarians knew about this parasite since it caused little or no disease [3]. Therefore, it was considered as an infrequent and insignificant pathogen.

The situations then had changed until the late 1970s and early 1980s due to the epidemic of acquired immunodeficiency syndrome (AIDS). The first human infection case was described in a 3-year-old child with acute and self-limiting gastroenteritis in 1976 [4]. In the same year, infectious cases were also reported in an immunocompromised patient [5] and young ruminants [6]. Fifty-eight (58) other cryptosporidiosis cases were then reported worldwide within 1976 to 1984, in which 40 cases (69%) occurred in either immuno-suppressed or compromised individuals. Of these 40 patients, 33 (83%) were human immunodeficiency virus (HIV) positive patients and 22 (55%) died [7-9]. The infection among individuals with a functional immune system is usually self-resolved but is persistent and fatal to patients with compromised or

weakened immunity (HIV/AIDS), which often involves infections of the hepatobiliary and the respiratory tracts in addition to the entire gastrointestinal tract [10-12]. Furthermore, reported cryptosporidiosis cases in animals have also been grown increasingly, which causes neonatal diarrhea in calves and lambs, gastritis in reptiles and fish, and respiratory diseases in birds [13-15]. Therefore, *Cryptosporidium* is regarded as not only an opportunistic pathogen in immunocompromised individuals, but also a significant pathogen in children and elderly, and in animals as well.

*Cryptosporidium* was soon becoming a public health concern and sparked great government and public interest because of several notable water-borne outbreaks in the same period of time. The largest documented waterborne outbreak in U.S. history happened in Wisconsin in 1993, caused by the failure of drinking water supply. In this outbreak, there were 403,000 people got sick, 4,400 people hospitalized, and more than 100 people died. The estimated direct and indirect economic costs associated with the outbreak was $96.2 million in total [16, 17]. The waterborne outbreaks of cryptosporidiosis are attributed to the resistance of *Cryptosporidium* oocysts to the chlorine disinfectants used for treating drinking and recreational waters, which also prompted the search for alternative disinfection technologies. The use of ozone and ultraviolet (UV) irradiation could be included in municipal water systems to diminish the vulnerability of cryptosporidial transmission via drinking water systems, but contamination of recreational water still plays an important role in the epidemiology of cryptosporidiosis [18-21]. Since water-borne cryptosporidiosis could potentially immobilize cities, and chemically resistant oocysts of zoonotic *C. parvum* could be easily acquired (such as from calves), *Cryptosporidium* was considered as a Category B priority agent in the national biodefense

program by the National Institutes of Health (NIH) and Centers for Disease Control and Prevention (CDC) in the U.S.

### 1.2. Taxonomy

Currently, there are at least 30 valid *Cryptosporidium* species and a number of genotypes with undefined species names known to infect a wide range of hosts, including humans, other mammals, birds, fishes and reptiles (**Table I-1**) [22]. Twenty-two (22) species infect mammals, including *C. muris*, *C. parvum*, *C. wrairi*, *C. felis*, *C. andersoni*, *C. canis*, *C. hominis*, *C. suis*, *C. bovis*, *C. fayeri*, *C. macropodum*, *C. ryanae*, *C. xiaoi*, *C. ubiquitum*, *C. cuniculus*, *C. tyzzeri*, *C. viatorum*, *C. scrofarum*, *C. proliferans*, *C. erinacei*in, and *C. rubeyi*. Other known species include four in birds (*C. meleagridis*, *C. baileyi*, *C. galli* and *C. avium*), two in fishes (*C. molnari* and *C. huwi*), two in reptiles (*C. serpentis* and *C. varanii*), and one in amphibians (*C. fragile*) (**Table I-1**). There are also over 50 distinguished genotypes, for which species names remain to be established or validated [23, 24].

Among them, *C. parvum* and *C. hominis* are the two major species associated with majority of clinically relevant human infections, in which *C. parvum* is zoonotic, while *C. hominis* is mainly human-specific [25]. However, a number of other species might also infect humans, mainly in immunocompromised patients (e.g., *C. wrairi*, *C. meleagridis*, *C. saurophilum* and *C. felis*) [26].

**Table I-1 The size of 30 currently established *Cryptosporidium* species***

| Species | Major host | Human pathogen** | Size of oocysts (μm) L × W | References |
|---|---|---|---|---|
| *C. andersoni* | Cattle | Yes (+) | 7.4 (6.0–8.1) × 5.5 (5.0–6.5) (*n* = 50) | Lindsay et al. [27] |
| *C. muris* | Rodents | Yes (++) | 6.1 (5.6–6.4) × 8.4 (8.0–9.0) (*n* = 25) | Palmer et al. [28] |
| *C. proliferans* | Rodents | No | 7.7 (6.8–8.8) × 5.3 (4.8–6.2) (*n* = 100) | Kvac et al. [29] |
| *C. avium* | Birds | No | 6.26 (5.30–6.90) × 4.86 (4.30–5.50) (*n* = 100) | Holubova et al. [30] |
| *C. baileyi* | Birds | No | 6.2 (5.6–6.3 × 4.6 (4.5–4.8) (*n* = 25) | Current et al. [31] |
| *C. bovis* | Cattle | Yes (+) | 4.89 (4.76–5.35) × 4.63 (4.17–4.76) (*n* = 50) | Fayer et al. [32] |
| *C. canis* | Dogs | Yes (++) | 4.95 (3.68–5.88) × 4.71 (3.68–5.88) (*n* = 50) | Fayer et al. [33] |
| *C. cuniculus* | Rabbits | Yes (++) | 5.98 (5.55–6.40) × 5.38 (5.02–5.92) (*n* = 50) | Robinson et al. [34] |
| *C. erinaci* | Hedgehogs, horses | Yes (+) | 4.9 (4.5–5.8) × 4.4 (4.0–4.8) (*n* = 100) | Kvac et al. [35] |
| *C. fayeri* | Marsupials | Yes (+) | 4.9 (4.5–5.1) × 4.3 (3.8–5.0) (*n* = 50) | Ryan et al. [36] |
| *C. felis* | Cats | Yes (++) | 4.6 (3.2–5.1) × 4.0 (3.0–4.0) (*n* = 40?) | Sreter et al. [37] |
| *C. fragile* | Toads | No | 6.2 (5.5–7.0) × 5.5 (5.0–6.5) (*n* = 50) | Jirku et al. [38] |
| *C. galli* | Birds | No | 8.25 (8.0–8.5) × 6.3 (6.2–6.4) (*n* = 50) | Ryan et al. [39] |
| *C. hominis* | Humans | Yes (+++) | 5.2 (4.4–5.9) × 4.9 (4.4–5.4) (*n* = 100). | Morgan-Ryan et al. [40] |
| *C. macropodum* | Marsupials | No | 5.4 (5.0–6.0) × 4.9 (4.5–6.0) (*n* = 50) | Power and Ryan [41] |
| *C. meleagridis* | Birds | Yes (++) | 5.0 (4.5–6.0) × 4.4 (4.2–5.3) | Sreter et al. [37] |
| *C. parvum* | Cattle, sheep, goats, horses, humans | Yes (+++) | 5.0 (4.5–5.4) × 4.5 (4.2–5.0) (*n* = 50) | Upton and Current [42] |
| *C. rubeyi* | Squirrels | No | 4.67 (4.4–5.0) × 4.34 (4.0–5.0) (*n* = 220) | Li et al. [43] |
| *C. ryanae* | Cattle | No | 3.73 (2.94–4.41) × 3.16 (2.94–3.68) (*n* = 0) | Fayer et al. [44] |
| *C. scrofarum* | Pigs | Yes (+) | 5.16 (4.81–5.96) × 4.83 (4.23–5.29) (*n* = 400) | Kvac et al. [45] |
| *C. serpentis* | Snakes | No | 5.94 (5.82–6.06) × 5.11 (5.03–5.19) (*n* = 37) | Xiao et al. [46] |

**Table I-1 Continued**

| Species | Major host | Human pathogen** | Size of oocysts (µm) L × W | References |
|---|---|---|---|---|
| *C. suis* | Pigs | Yes (+) | 4.6 (4.4–4.9) × 4.2 (4.0–4.3) (*n* = 50) | Ryan et al. [47] |
| *C. tyzzeri* | Mice | Yes (+) | 4.64 ± 0.05 × 4.19 ± 0.06 (*n* = 69) | Ren et al. [48] |
| *C. ubiquitum* | Sheep, deer, rodents, primates | Yes (++) | 5.04 (4.71–5.32) × 4.66 (4.33–4.98) (*n* = 50) | Fayer et al. [49] |
| *C. varanii* | Lizards | No | 4.94 (4.81–5.07) × 4.49 (4.35–4.63) (*n* = 20) | Xiao et al. [46] |
| *C. viatorum* | Humans | Yes (++) | 5.35 (4.87–5.87) × 4.72 (4.15–5.20) (*n* = 50) | Elwin et al. [50] |
| *C. wrairi* | Guinea pigs | No | 5.4 (4.8–5.6) × 4.6 (4.0–5.0) | Tilley et al. [51] |
| *C. xiaoi* | Sheep | Yes (+) | 3.94 (2.94–4.41) × 3.44 (2.94–4.41) (*n* = 25). | Fayer and Santin [52] |
| *C. huwi* | Fish | No | 4.6 (4.4–4.9) × 4.4 (4.0–4.8) (*n* = 50) | Ryan et al. [53] |
| *C. molnari* | Fish | No | 4.72 (3.23–5.45) × 4.47 (3.02–5.04) (*n* = 22) | Alvarez-Pellitero and Sitja-Bobadilla [54] |

* Data obtained and adapted from Xiao and Cama, 2018 [22]; ** Note: +++, major human pathogen; ++, relatively common in humans; +, confirmed infections have been detected in a small number of patients.

### 1.3. Transmission and risk factors

*Cryptosporidium* infection is mainly transmitted through the fecal-oral route, either by direct contact with infected persons or animals, or by consumption of contaminated water or food [55-57]. Direct transmission is likely to be considerable factors to the prevalence of cryptosporidiosis, whether zoonotic (animal-to-human transmission) or anthroponotic (person-to-person transmission) [58]. In particular, the prevalence of cryptosporidiosis in daycare centers and households in developed countries illustrates the importance of direct person-to-person transmission [59-62]. In most case-control studies, exposures to farm animals (especially calves)

are one of the major risk factors for cryptosporidiosis [63-65]. Indirect transmission mainly depends on the mechanical transmission of oocysts, resulting in a significant threat to those developing countries [66-68]. As oocysts are resistant to disinfectants such as chlorine used in water treatments, epidemiologic studies have identified water as a major route responsible for indirect transmission. Numerous outbreaks of cryptosporidiosis have been attributed to contaminated drinking water [69, 70]. Additionally, the incidence of cryptosporidiosis also influenced by factors like season, surface water concentrations, vegetation cover, animal husbandry, and hygiene practices [68, 71-73].

### 1.4. Pathogenesis and cryptosporidiosis

Cryptosporidiosis is a term to describe the infectious disease caused by *Cryptosporidium* species. The parasites are typically found on the microvillus border of epithelial cells, most commonly in the small intestine. Upon ingestion by a host, the oocysts undergo excystation to release sporozoites that attach to the surface of the host cells prior to invasion. During the invasion of a sporozoite, a parasitophorous vacuole membrane (PVM) is formed via extension of host cell membrane at the infection site to cover the invading sporozoite, followed by transformation of the sporozoites into trophozoites and subsequent intracellular development. The replication of parasite takes place within the PVM, including 2 or more cycles of merogony (asexual developmental stages) and gametogony (sexual developmental stage). After fertilization between macrogametes and microgametes, two types of new oocysts are formed, i.e., thick-walled (80%) and thin-walled (20%) oocysts. Both types of oocysts are sporulated before being released from host cells. Thick-walled oocysts are typically released into the environment and are infectious immediately after excretion for invading new hosts, whereas thin-walled oocysts

may excyst within the same host, resulting in autoinfection [74, 75]. Auto-infection is believed to be the mechanism of persistent infections in immunocompromised individuals (e.g., HIV-positive/AIDS patients) in the absence of repeated exposures to the oocysts in the environments [14, 76]. As the life cycle occurs mostly at the luminal surface of the mucosal epithelial cells, the parasites are viewed as a "minimally invasive" mucosal pathogen [25].

Depend on the parasite species and immunocompetency of a host, *Cryptosporidium* infection can even involve in epithelial cells of the biliary tract, stomach, esophagus, and even respiratory tract [77]. In animals, with the exception of cryptosporidiosis in chickens usually manifests as respiratory disease, *Cryptosporidium* normally causes intestinal tract infection to the young associated with illness, including diarrhea leads to dehydration, inappetence, weight loss, fever, and moderate mortality [13, 78, 79]. Actually, there is not much difference between the symptoms of animals and human cryptosporidiosis. Although some *Cryptosporidium* infections are asymptomatic, in symptomatic infections, patients may suffer from stomach cramp, vomiting, fever and nausea, to weight loss. The most common and notable clinic outcome of cryptosporidiosis in humans and other mammals is the watery diarrhea, which generally begins a few days or a week after infection [9, 75, 76]. Cryptosporidial infections in immunocompetent individuals are usually self-limiting, and patients may recover after one week or two after infection. However, cryptosporidiosis can be chronic and severe in immunocompromised patients. In children under age of 5, cryptosporidiosis may result in malnutrition and delayed growth, and is associated with decreased survival in infants and toddlers in developing countries as well [10, 68, 80-82].

## 1.5. Treatment

The current options to treat cryptosporidiosis are limited. The progress in developing novel anti-cryptosporidial therapeutics has been slow. The major obstacles impeding the drug discovery include the limitations of in vitro culture of *Cryptosporidium*, difficulties to genetically manipulate the organism, and the unique metabolic features in this parasite (e.g., the lack of many classic drug targets due to its highly streamlined metabolism) [83-87]. Currently, nitazoxanide (NTZ) is the only drug licensed by the Food and Drug Administration (FDA) for treating immunocompetent patients including adults and children >12 months of age. However, NTZ is not fully effective against cryptosporidiosis, and is known to be ineffective in immunocompromised patients [88]. Therefore, there is an urgent need for developing new anti-cryptosporidial therapeutics.

### *1.5.1 Current treatment options*

Nitazoxanide (NTZ) is a thiazole compound and is well-known for its broad-spectrum activity against a number of intestinal protozoa and anaerobic bacteria. NTZ is the only FDA-licensed drug recommended for treating cryptosporidiosis in immunocompetent patients (adults and >1-year-old children), but it is ineffective in immunocompromised individuals [89, 90]. The approval of NTZ for cryptosporidiosis was mainly based on several randomized clinical trials in HIV-negative participants. The efficacy of NTZ in immunocompetent patients (50 adults and 50 children) was examined by a randomized, double-blind placebo-controlled clinical study in Egypt. It showed that significant clinical and parasitological cure rates up to 80% compared to placebo (41%) followed by a 3-day treatments in adults, adolescents and children (1-3 years and 4-11 years of age groups, respectively) [91]. Additionally, the same course of treatment also applied in patients 12 years of age or older showed a statistical significance ($P < 0.0001$) in both

the duration of diarrhea and oocyst shedding [89]. However, two randomized controlled trials in Zambian showed no efficacy of NTZ on cryptosporidial infections in HIV-positive children, even with the use of high doses and prolonged treatments [90, 92].

Additionally, the anti-cryptosporidial activity of NTZ remains unclear in adult AIDS patients. There was a placebo-controlled study showing that a 2-week treatment with NTZ (500 mg to 1000 mg twice a day) led to a better than placebo parasitological cure in adult HIV patients (63% parasitological cure in patients receiving 1 g/d and 67% in patients receiving 2 g/d of NTZ; vs. 25% in patients receiving placebo). Complete diarrheal syndrome was resolved in 86% patients who were considered parasitological cured in comparison with 50% patients receiving placebo [93]. Meanwhile, patients with $CD4^+$ T-cell counts at >50 cells/$mm^3$ in the response rates of both dose groups were superior to those with counts at <50 cells/$mm^3$. Therefore, NTZ was more effective in patients with lighter cryptosporidial infections than those with moderate-to-heavy infections [93, 94]. It is obvious that NTZ is inadequate for treating cryptosporidiosis in immunocompromised patients, and novel anti-cryptosporidial therapies for improving parasitological responses are needed. Several other marketed drugs have also been described with activity against *Cryptosporidium* in vitro, in vivo and/or in patients, including paromomycin, azithromycin, and rifaximin [95-98]. However, none of them has received FDA approval for treating cryptosporidiosis, and clinically showed inefficacy on cryptosporidiosis in AIDS patients [10, 99, 100].

There is also a lack of FDA-approved drugs for treating cryptosporidiosis in animals. In some other countries, halofuginone lactate (Halocur) is approved for veterinary use to treat cryptosporidiosis in calves and lamb and coccidiosis caused by *Eimeria* parasites in poultry. Halofuginone lactate is a synthetic compound derived from a plant quinazolinone alkaloid from

*Dichroa febrifuga* (Chinese herb, Chang Shan). Despite reports of potent anti-*Crypto*sporidium efficacy has been described, halofuginone lactate is not fully effective in eliminating oocyst productions in animals. One study shows that in naturally infected calves, both halofuginone lactate and paromomycin exhibited a decrease in the severity of diarrhea but a limitation in infection eradication. This study included two treatment groups of calves between 7 and 12 days of ages that were administrated with halofuginone lactate and paromomycin at 100 μg/kg/day and 100 mg/kg/day, respectively for 7 days. Both treatment groups showed decreases in oocyst shedding from day 1 after receiving treatment, and a statistically significant decrease of oocyst shedding was observed from day 3 ($P < 0.05$) [101]. Although approved for use in animals, halofuginone lactate is prohibited for use in humans due to its significant hepatotoxicity and gastrointestinal side effects [86, 102-104].

### *1.5.2 Ongoing drug discovery and novel compounds*

Two approaches are commonly employed to identify new compounds with activity against infectious diseases. The first one uses traditional methods that directly screens chemical entities for activities against an in vitro or in vivo model of infection. The second one uses target-based methods that screens compounds against defined molecular targets in a pathogen, such as essential enzymes or receptors. As discussed above, there had been a number of obstacles hampering the discovery and development of anti-cryptosporidial drugs. For example, in vitro cultivation of *C. parvum* in human colonic tumor 8 cells (HCT-8) or human colonic adenocarcinoma cells (Caco-2) were established a few decades ago [105-108], but the in vitro systems were not suitable for high-throughput screening (HTS) of drugs against the cultured parasite. However, in the past decade or two, increasing efforts in *Cryptosporidium* research have led to several significant advancements in understanding the biology of the parasite and in

developing new tools to study the parasite. One of them is the establishment of cell-based screening platforms in high throughput format. Together with the availability of chemical libraries from commercial sources or from private collections, it became achievable to conduct phenotypic HTS of drugs against the growth of *C. parvum* and large-scale evaluation of drug efficiency in vitro [108-110]. The availability of genome sequences of several *Cryptosporidium* species (e.g., *C. parvum* and *C. hominis*) allows the identification of new molecular targets in the parasites for target-based drug discovery [12, 83, 111-113].

One of the HTS platforms was based on high-content imaging analysis that has been used to screen 727 FDA-approved drugs ($Z' = 0.21$-$0.47$) and discovered anti-cryptosporidial activity of HMG-CoA reductase inhibitors [114]. The assay was also used to screen 400 compounds from the Medicines for Malaria collection and identified 19 compounds with significant efficacy against *C. parvum* at 6.6 uM [115]. Another HTS assay was based on quantitative RT-PCR (qRT-PCR), in which high-throughput was achieved by directly using cell lysates as the templates to give excellent uniformity and signal-noise ratios (i.e., >150-fold linear dynamic range in detecting the parasite loads; $Z' = 0.73$-$0.87$) [108]. The assay was used to screen a collection of 1200 marketed drugs and identified a number of hits and leads with excellent efficacies against cryptosporidial infection in vitro and in vivo (e.g., vorinostat) [116]. A genetically engineered *C. parvum* strain containing nanoluciferase was also employed for drug screening in vitro and drug efficacy evaluation in vivo, including a phenotypic screening of 6,220 compounds in vitro, which lead to an identification of 154 compounds exhibiting > 60% inhibition against both *C. parvum* and *C. hominis* at 5 μM [117].

An increasing effort in the past decades has also led to discovering new promising leads with defined molecular targets in the parasite. Examples include: compound 1294 on calcium

dependent protein kinase (CDPK) [118]; compound P131 on inosine-5'-mono-phosphate dehydrogenase IMPDH [119]; vorinostat on histone-deacetylase (HDAC) [116]; and pyrazolopyridines (e.g., KDU731) on lipid kinase PI(4)K (Phosphatidylinositol-4-OH kinase) [117]. These lead compounds are mostly under the preclinical stages of investigation, representing significant advancements in anti-cryptosporidial drug discovery and development.

### 1.6 Natural products

In the past decades, natural products and their derivatives have been receiving increasing attention by the infectious disease community for discovering new therapeutics and as an alternative strategy to conquer antibiotic resistance [120-122]. The history of using medicinal plants to treat parasitic diseases could be traced back to the ancient times. Since 19$^{th}$ century when pure compounds as active principles in plants were discovered and described, the exploitation of natural products became part of the molecular sciences. Many of the current antibiotics or drugs are in fact natural products, such as camptothecin, reserpine, silibinin, berberine and curcumin[123-126]. Quinine as one of the oldest antimalarial drugs, first isolated from *Cinchona* plants (Rubiaceae) in 1820, is still in use today. It represents a milestone in the history of discovering antiparasitic drugs from the nature [127]. Another world-famous antimalarial drug, artemisinin (qinghaosu), which won the Nobel Prize in Physiology or Medicine in 2015, is also a natural product from plant *Artemisia annua* [128].

Nowadays, the terminology of natural products not only refers as traditional or ethnic medicine, but has been expanded to include products from bacteria, fungi and plants to protozoa, sponges and invertebrates found in a variety of environments (e.g., deep sea, rainforests and hot springs). Research on natural products now becomes a highly active field attracting the attention

from academia to the pharmaceutical industry and all the major related stakeholders worldwide [129, 130] .

However, in contrast to the study in chemical compounds, existing research on the efficacy of natural products against *Cryptosporidium* has been mostly sporadic, and the selection of natural products or extracts was typically arbitrary. For this reason, highly efficacious anti-cryptosporidial natural products have yet been truly discovered. There are a very few reported studies to explore the efficacy of natural products and derivatives against *Cryptosporidium*, e.g. 1) curcumin, a natural polyphenolic compound isolated form turmeric (*Curcuma longa*), showed a certain activity against *C. parvum* in vitro; 2) garlic (*Allium sativum*) was efficacious against cryptosporidial infection in experimentally infected immunocompetent and immunosuppressed mice; and 3) Pine bark extract (Pycnogenol) was reported for use as a dietary supplement for *C. parvum*-infected patients [131-133].

In a recent study, Jian-Jun and colleagues screened 3,127 fractions from 159 microbial strains for activities against *C. parvum* infection in HCT-8 cells and identified 6 herbicidin congeners from *Streptomyces sp.* CB01388 with moderate activity against *C. parvum* with no toxicity to host cells [134]. In another study, plant flavonoid aurone and its derivates, which provide yellow color to some flowers and share structural similarity to chalcones, have been reported for showing capacity to against the intracellular growth of *C. parvum* with little-to-moderate toxicity to host cells [135].

### 1.7 Drug combinational therapy

There has been a long history of exploring drug combinations with many successful stories in human medicine. Traditional Chinese medicine commonly uses mixtures of herbs for

treating diseases, which was considered as the earliest documented use of multi-compounds therapy [136]. Since the last century, advances in molecular biology have greatly promoted our understanding of the combined use of active ingredients from herbs. The advancements in omics and cell biology have explained that a disease is actually a disturbed system of interconnected molecular pathways. From this perspective, it is easier to understand that the simultaneous action of several drugs may potentially provide more effective treatments [137-139].

There is a growing interest in the pharmaceutical industry in the discovery and development of combination therapies, especially in cancer chemotherapy. There is also an increasing awareness that synergistic drug combinations may have the potential to increase therapeutic efficacy, reduce toxicity of drugs, and/or lower side effects [140]. The effect of two compounds, when applied together, cause a greater response than expected based on their individual potencies and efficacies may be synergistic (super-additivity); effect may show antagonism (sub-additivity) or simple additivity as well [141]. Nowadays, combination therapies have been commonly accepted as standard treatment options for a number of infectious diseases and cancers [142-144] and continues to represent a promising approach to potentially address some unmet medical needs [139].

In recent years, efforts to find chemotherapeutic treatments of cryptosporidiosis have been mainly initiated on identification and evaluation of anti-cryptosporidial efficacy of single hits or leads. Drug combinations are generally under-appreciated in cryptosporidiosis research. There were only a few reported studies that evaluated anti-cryptosporidial efficacies of drug combinations. In one study, the combination of NTZ (8 mg/L) with both azithromycin (8 mg/L) and rifampin (8 mg/L) in vitro suppressed growth of *C. parvum* by 83.9% and 79.8%, respectively, compared with 56.1% when used alone [145]. A research group in Egypt reported a

significant reduction on oocyst shedding when NTZ and phenyl vinyl sulfone (PVS) were used together in *C. parvum*-infected mice [146]. In another study, reductions on stool frequency and oocyst shredding were observed in AIDS patients with combination therapy of paromomycin and azithromycin [147]. A study on farm animals exhibited that the combination of metronidazole (1,000 mg twice daily) and furazolidone (500 mg twice daily) was highly effective, leading to no sign of diarrhea after 5-day treatment and no detection of oocysts in fecal samples on day 7 post treatment [148].

Considering the above existing researches and facts of lacking fully effective treatments and availability of only a few "partially" effective existing drugs or compounds, it is worthy of exploring the potential to improve the anti-cryptosporidial efficacy via drug combinations.

In the present study, we aimed to discover new anti-cryptosporidial structures by in vitro phenotypic screening of 800 pure natural products and derivatives and to evaluate the potential of synergy of anti-cryptosporidial efficacies by combining drugs targeting different pathways in the parasite.

# CHAPTER II

# DISCOVERY OF NOVEL ANTI-CRYPTOSPORIDIAL ACTIVITIES FROM NATURAL PRODUCTS BY IN VITRO HIGH-THROUGHPUT PHENOTYPIC SCREENING *

## 2.1 Introduction

*Cryptosporidium parvum* (Phylum Apicomplexa) is a zoonotic protozoan parasite causing cryptosporidiosis in humans and animals. In humans, *C. parvum* infection can result in mild to severe watery diarrhea that is usually self-resolved in a couple of weeks in immunocompetent individuals, but could be chronic and deadly in immunocompromised patients [25, 149, 150]. In developing countries, *Cryptosporidium* is one of the top agents causing diarrhea and associated with stunted growth and increased fatality in children [150-154]. It is also an important water-borne and food-borne pathogen, frequently causing cryptosporidiosis outbreaks around world. In the United States alone, there was an earlier estimation of 748,000 annual cases of cryptosporidiosis [155, 156]. Historically, the number of reported cases of cryptosporidiosis in the United States caused by contaminated water and food increased from 7,656 in 2009 to 9,313 in 2011; and then decreased to 8,008 in 2012 [155, 157]. A more recent analysis of 7,465 cases in the period of 2009–2017 in the United States showed that ingestion of recreational water (e.g., pools and water playgrounds) was the predominant risk factors responsible for 35.1% outbreaks and 56.7% cases [158]. In farm animals, *Cryptosporidium* is an important pathogen responsible for the neonatal diarrhea syndrome of calves, lambs and other

young ruminants, resulting in considerable direct and indirect economic losses [13]. However, current treatment options for cryptosporidiosis are limited [115]. No drugs are FDA-approved for treating cryptosporidiosis in animals in the United States, while nitazoxanide (NTZ) is the only drug approved by FDA for treating cryptosporidial infection in immunocompetent human patients, but not in people with compromised immunity [89, 90, 99, 159, 160].

Besides NTZ, a few other marketed drugs including paromomycin and azithromycin possess certain levels of anti-cryptosporidial activity, but they are not FDA-approved for treating cryptosporidiosis [114, 161-163]. More recently, several promising anti-cryptosporidial lead compounds have been reported with low nanomolar activity in vitro and low mg/kg activity in animal models, such as the compound 1294 acting on calcium dependent protein kinase (CDPK) [118], P131 on inosine-5'-mono-phosphate dehydrogenase IMPDH [119], KDU731 on phosphatidylinositol-4-OH kinase (PI(4)K) [117], triacsin C on acyl-CoA synthetase (ACS) [84] and SAHA on histone-deacetylase (HDAC) [116]. They are still in the lead optimization or pre-clinical stages of development. Therefore, there is an urgent need to discover new anti-cryptosporidial compounds, particularly those with the potential for use in young and immunocompromised patients and animals [10].

Natural products are virtually an unlimited source of highly diversified chemical structures for discovering various medicinal activities. Many antibiotics and drugs are in fact natural products, such as camptothecin, lovastatin, quinine and silibinin [124-126, 164]. The Nobel Prize-winning anti-malarial drug, artemisinin (qinghaosu), is a natural product from plant *Artemisia annua L.* [165]. Due to the lack of high-throughput screening system in earlier days, there had been only a few reports on evaluating of anti-cryptosporidial activity of selected non-microbial natural products or plant extracts (e.g., [131, 132, 166-170]).

In the present study, we took advantage of our recently developed qRT-PCR assay for high-throughput screening (HTS) of anti-cryptosporidial drugs [108], and screened a total of 800 structurally diverse natural products for their activities against the growth of *C. parvum* in vitro. We discovered more than 16 natural products showing low to sub-micromolar anti-*C. parvum* activity, and analyzed the action of 3 compounds for their activity on various developmental stages of *C. parvum* in more detail. Our findings provide a set of new chemical structures as anti-cryptosporidial hits for further investigations.

## 2.2 Materials and methods

### *2.2.1 In vitro culture of C. parvum*

The culture of *C. parvum* in vitro and drug screening were performed as described [108, 116]. Briefly, fresh oocysts of *C. parvum* (BGF-1 strain; subtype IIaA17G2R1) were purchased from Bunch Grass Farm (Deary, ID), purified using a Percoll-based gradient centrifugation method and sterilized with 10% bleach for 7 min on ice, followed by extensive washes with phosphate-buffered saline (PBS). Oocysts less than 3 months old since harvest were used in all experiments. The strain of *C. parvum* was originally described as Iowa-1 strain (subtype IIaA15G2R1), but has been replaced by a new strain with a subtype IIaA17G2R1. For clarity, we have renamed it as BGF-1 strain.

Host cells used HCT-8 cell line derived from a human ileocecal adenocarcinoma (American Type Culture Collection # CCL-225). HCT-8 cells were seeded in 96-well plate at a density of 23,000 cells/well and allowed to grow overnight in 200 µL RPMI-1640 medium with 10% fetal bovine serum (FBS) at 37 °C under 5% $CO_2$ atmosphere. After cell monolayers reached to 80-90% confluence, plates were incubated with *C. parvum* oocysts (20,000

oocysts/well) for 3 h, and uninvaded parasites were removed by a medium exchange. Compounds at designed concentration and diluent were added at this point. Parasite-infected cells were cultured for additional 41 h (total 44 h infection time) and lysed at this time point for qRT-PCR as described below.

### *2.2.2 qRT-PCR assay*

The relative levels of *C. parvum* were determined by detecting the levels of 18S rRNA transcripts (Cp18S), normalized with those of host cell 18S rRNA transcripts (Hs18S) by qRT-PCR. After 44 h post-infection (hpi) time, plates were gently washed 3 times with PBS, followed by the addition of 150 μL ice-cold Bio-Rad iScript qRT-PCR sample preparation regent (lysis buffer) (Bio-Rad Laboratories, Hercules, CA). Plates were sealed with adhesive and heat-sealing films and vortexed in a bucket containing ice for 20 min in a plate vortexer (VX-2500, VWR International, Radnor, PA; speed at 7). The plates were centrifuged (5 min, 2000 × g) to ensure all the debris were attached to the bottom of the wells and then incubated at 75 ºC for 15 minutes. The supernatants are either stored at -80 ºC or directly used for qRT-PCR.

For qRT-PCR detection, the lysates were diluted by 100 and 2000 folds for detecting Cp18S and Hs18S transcripts, respectively, using a qScript one-step SYBR green qRT-PCR kit (Quanta Biosciences, Gaithersbury, MD). Hs18S levels were used as controls and for normalization. The qRT-PCR reactions were carried out in 384-well plates in a CFX384 Touch Real-Time PCR Detection System (Bio-Rad Laboratories). Each well contained 10 μL reaction solution mixed with 3 μL diluted cell lysate, 5 μL one-step SYBR green master mix, 0.2 μL RT master mix, and primers for Cp18S (i.e., Cp18S-1011F, 5′-TTG TTC CTT ACT CCT TCA GCA C-3′ and Cp18S-1185R, 5′- TCC TTC CTA TGT CTG GAC CTG-3′; 200 nM) or Hs18S transcripts (i.e., Hs18S-1F, 5′-GGC GCC CCC TCG ATG CTC TTA-3′ and Hs18S-1R, 5′-CCC

CCG GCC GTC CCT CTT A-3′; 700 nM). The cycle threshold ($C_T$) were recorded for computing relative parasite loads based on $\Delta\Delta C_T$ values.

During the course of this study, standard curves derived from specimens infected with various numbers of *C. parvum* were produced for new batches of parasites and reagents for assessing the PCR amplification efficiency, i.e., calculation of the parameter **A** by linear regression between $C_T$ values and the logarithm of inoculated oocyst numbers (**A** = 1/**Slope**). A percent inhibition of parasite growth could be calculated using following equation as described [106, 108]:

$$Inhibition\ (\%) = (1 - 10^{A \cdot \Delta\Delta C_T}) \cdot 100 \qquad (1)$$

In comparison with the following simplified empirical equation that assumes perfect PCR amplification efficiency:

$$Inhibition\ (\%) = (1 - 2^{-\Delta\Delta C_T}) \cdot 100 \qquad (2)$$

We have noticed that the percent inhibition obtained using Eq. (2) would be generally slightly lower that that obtained using standard curve-based Eq. (1). Because a slight under-estimation of inhibition in fact makes the drug efficacy data more conservative, we hence used the simplified Eq. (2) in all calculations in this study.

### *2.2.3 In vitro screening of natural products*

The NatProd Collection containing 800 pure chemicals of natural products were purchased from MicroSource Discovery Systems (http://www.msdiscovery.com) for discovering potential activities against the growth of *C. parvum* in vitro using qRT-PCR assay as described above. The primary screening was carried out for all 800 compounds at 10 μM containing 0.5% dimethyl sulfoxide (DMSO). In each 96-well plate, six wells were treated with 0.5% DMSO diluent as negative control, and two wells were treated with paromomycin at 150 μM as positive

control. Secondary screening was conducted on compounds showing ≥ 60% inhibition on the parasite growth in primary screening at concentrations of 10 μM and 3.3 μM with the same experimental design as in the primary screening. Compounds showing ≥ 50% inhibition at 3.3 μM in the secondary screening were tested for dose-response curves to determine their $EC_{50}$ values (half maximal effective concentration against the growth of *C. parvum* in vitro). All experiments included least two biological replicates for each compound in the in vitro drug treatment assay and two technical replicates for each biological replicate in the qRT-PCR assay. All primary and secondary screening assays were performed at least twice independently. For compounds showing disparities between replicates or experiments, the assays were repeated until data were convergent.

### *2.2.4 Effect of top hits on different parasite developmental stages in vitro and drug withdrawal assay*

We selected three top hits derived from plants for evaluating their activity against various developmental stages of *C. parvum.* For evaluating the effect on the parasite invasion (i.e., 0-3 hpi treatment groups), host cell monolayers will be incubated with *C. parvum* oocysts ($10^5$ oocysts/well) in 96-well plates together with individual compounds at around $EC_{80}$ concentrations. For evaluating the effect on various stages of intracellular parasites (i.e., 3-10 hpi, 3-20 hpi, 22-44 hpi and 3-44 hpi treatment groups), host cell monolayers were incubated with *C. parvum* oocysts (50,000 oocysts/well) for 3 h, followed by the removal of uninvaded parasites by a medium exchange. Individual compounds at $EC_{80}$ final concentrations were added into wells at specified post-infection time points, and plates were incubated for specified durations of post-infection times. Cell lysates were prepared at the end of each treatment for qRT-PCR.

For drug withdrawal assay, HCT-8 cells were cultured and inoculated with *C. parvum* oocysts (50,000 oocysts/well) for 3 h. After a medium exchange, individual compounds at $EC_{80}$ final concentrations were added into wells. Compounds were removed at 22 hpi time point by a medium exchange, and infected cells were allowed to grow up to 44 hpi (3-22 hpi treatment groups). A full course of treatment for each compound was included as control (3-44 hpi treatment groups). Cell lysates were prepared at 44 hpi time point for qRT-PCR.

In all experiments, negative controls were treated with diluent (0.5% DMSO) for the same durations of corresponding drug treatment groups. All experiments include least three biological replicates for each compound in the in vitro drug treatment assay and two technical replicates for each biological replicate in the qRT-PCR assay.

### *2.2.5 In vitro cytotoxicity assay*

Cytotoxicity of top hits on host cells was evaluated by an MTS assay (aka. one-step MTT assay) [171]. In this assay, HCT-8 cells were cultured in 96-well plates overnight, followed by incubation with compounds at serially diluted concentrations for 41 h. Plates were then rinsed 3 times with PBS, and incubated with a CellTiter 96 AQueous One Solution Cell Proliferation Assay (MTS) solution (20 μL/well) at 37°C for 90 min in a 5% $CO_2$ incubator according to the manufacturer's protocol (Promega, Madison, WI). The plates were measured for absorbance at 490 nm in 15 min intervals in a SmartReader 96 microplate reader (Accuris, Edison, NJ). Cytotoxicity of a compound was quantified by calculating the half maximal inhibitory concentration on host cells ($TC_{50}$). An in vitro safety interval (SI) was calculated by determining the ratio between $TC_{50}$ and $EC_{50}$ values (i.e., $\mathbf{SI = TC_{50}/EC_{50}}$).

## 2.3 Results

### *2.3.1 Phenotypic HTS identified 16 natural products with lower micromolar to sub-micromolar activity against the growth of C. parvum in vitro*

In primary screening at 10 μM, we have observed a wide range of activity of the 800 natural products on the growth of *C. parvum* in vitro (i.e., ranging from −96.29% to 99.93% inhibitions) (**Figure II-1 and Supplementary Table A-1**). Based on Hs18S $\Delta C_T$ values between treatment and control groups, 20 compounds were highly cytotoxic to host cells at 10 μM and removed from the hit list. Among the remaining 780 compounds, we identified 88 compounds that inhibited the parasite growth by >60%. The 88 compounds were subjected to secondary screening at 10 and 3.3 μM, in which 29 compounds retained >50% inhibition activity at 3.3 μM (**Supplementary Table A-2**). Subsequent dose-response experiments identified 16 compounds out of the 29 hits that exhibited lower to sub- micromolar $EC_{50}$ values (i.e., $EC_{50}$ <4.0 μM) against the parasite growth in vitro (**Figure II-2** and **Table II-1**), which represents 2% of the 800 natural products in the NatProd collection.

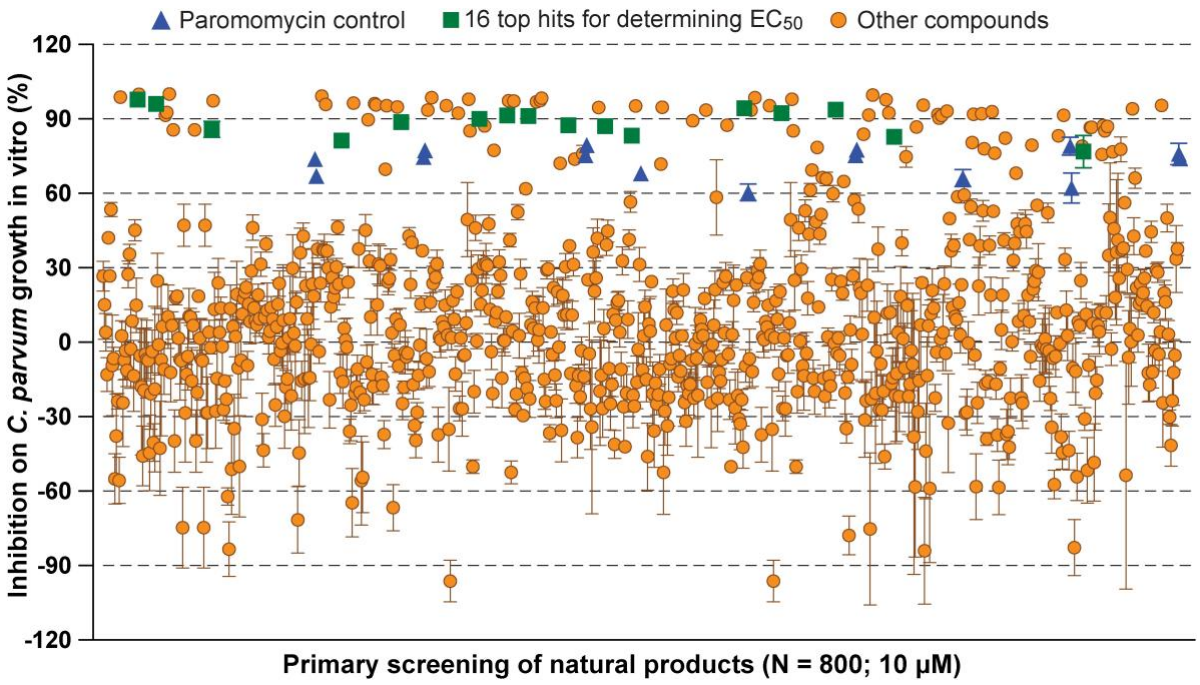



**Figure II-1 Scatter plot of the primary screening of 800 natural products (10 µM) against the growth of *Cryptosporidium parvum* in vitro.**
Blue triangles represent data from the positive control compound paromomycin (150 µM). Green squares represent the 16 top hits selected for determining their antiparasitic half maximal effective concentration ($EC_{50}$) values and cytotoxicity shown in **Table II-1** and **Figure II-2**. Each plate included 0.5% dimethyl sulfoxide diluent only as negative control (6 wells/plate). Bars show the standard error of the mean (N ≥3).

The anti-cryptosporidial $EC_{50}$ values of the 16 top hits ranged from 0.122 μM to 3.940 μM, in which 7 compounds had $EC_{50}$ values <1.0 μM (**Figure II-2** and **Table II-1**). Among the 7 top hits, three compounds were antibiotics derived from *Streptomyces* bacterial species, including valinomycin (#1 hit; $EC_{50}$ = 0.122 μM), mitomycin (#2 hit; $EC_{50}$ = 0.133 μM), and dactinomycin (#4 hit; $EC_{50}$ = 0.314 μM), while four compounds were derived plants, including cedrelone (#3 hit; $EC_{50}$ = 0.267 μM), deoxysappanone b 7,4'-dimethyl ether (Deox B 7,4) (#5 hit; $EC_{50}$ = 0.734 μM), tanshinone IIA (#6; $EC_{50}$ = 0.964 μM), and baicalein (#7; $EC_{50}$ = 0.981 μM) (**Table II-1**). The remaining 9 compounds with EC50 values ranging from 1.187 μM (deoxysappanone B 7,3'-dimethyl ether acetate) to 3.940 μM (3-deoxo-3beta-hydroxy-mexicanolide 16-enol ether) includes 7 derived from plants and two from microbes (**Table II-1**).

**Table II-1 In vitro anti-*Cryptosporidium* activity, cytotoxicity and safety interval (SI) of 16 top hits identified from 800 natural products [a]**

| Compound | Source (species) | CAS # | Description | $EC_{50}$ (μM) | $TC_{50}$ (μM) | SI [b] |
|---|---|---|---|---|---|---|
| Valinomycin | Microbe (*Streptomyces*) | 2001-95-8 | Antibiotic; cyclic peptide ionophore | 0.122 | >50 | >410 |
| Mitomycin | Microbe (*Streptomyces*) | 50-07-7 | Antibiotic, Antineoplastic; DNA synthesis inhibitor | 0.133 | 13.1 | 98.7 |
| **Cedrelone** | **Plant (*Toona ciliate*)** | **1254-85-9** | **antineoplastic** | **0.267** | **3.59** | **13.4** |
| Dactinomycin | Microbe (*Streptomyces*) | 50-76-0 | Antineoplastic; DNA-binding/RNA synthesis inhibitor | 0.314 | 2.82 | 9.10 |
| **Deoxysappanone B 7,4'-dimethyl ether (Deox B 7,4)** | **Plant (*Biancaea sappan*)** | **674786-37-9** | **Anti-leukemic; microtubule inhibitor** | **0.734** | **64.9** | **88.9** |
| Tanshinone IIA | Plant (Salvia miltiorrhiza) | 568-72-9 | Antineoplastic, bone resorption inhibitor, antiproliferative, apoptosis inducer, anti-inflammatory | 0.964 | >100 | >104 |
| **Baicalein** | **Plant (*Scutellaria*)** | **491-67-8** | **Antiviral (HIV), anti-inflammatory** | **0.981** | **>100** | **>102** |
| Deoxysappanone B 7,3'-dimethyl ether acetate | Plant (*Biancaea*) | 356.3788 | Human tyrosyl-DNA phosphodiesterase 1 inhibitor | 1.187 | >100 | >84 |
| Daunorubicin | Microbe (*Streptomyces*) | 20830-81-3 | Antibiotic, Antineoplastic | 1.494 | 42.6 | 28.5 |
| Dihydrogambogic acid | Plant (*Garcinia hanburyi*) | | Matrix metalloproteinase 1 inhibitor | 1.669 | 6.31 | 3.78 |
| Deacetylgedunin | Plant (*Azadirachta indica*) | 10314-90-6 | Antiplasmodial, anti-inflammatory | 1.771 | 30.9 | 17.4 |
| Deacetoxy-7-oxogedunin | Plant (*Carapa guianensis*) | 13072-74-7 | Antiplasmodial activity | 1.943 | 12.8 | 6.59 |
| Lovastatin | Microbe (*Aspergillus terreus*) | 75330-75-5 | Antihyperlipidemic, HMGCoA reductase inhibitor | 2.406 | >100 | >41.6 |
| Dihydrotanshinone I | Plant (*Salvia miltiorrhiza*) | 87205-99-0 | Used for treating cardiovascular diseases | 3.083 | 25.0 | 8.11 |
| 2,3,4'-Trihydroxy-4-methoxybenzophenone | Plant (*Anemarrhena asphodeloides*) | 260.24874 | Natural product derivative | 3.689 | >100 | >27.1 |
| 3-Deoxo-3beta-hydroxy-mexicanolide 16-enol ether | Plant (unknown) | 484.59492 | Natural product derviative | 3.940 | >100 | >25.4 |

[a] Compounds in bold fonts were subjected to further study of their effects on various parasite developmental stages; [b] SI = safety interval.

All 16 top hits were efficacious on *C. parvum* at concentrations non-toxic to HCT-8 host cells, with $TC_{50}$ ranging from 2.82 μM (dactinomycin) to >100 μM (6 compounds) (**Figure II-2** and **Table II-1**). Twelve compounds had in vitro safety intervals (SIs) greater than 10 (i.e., SI = 13.4 to >410), while four compounds had lower SI values (i.e., SI = 4.52 to 9.10).

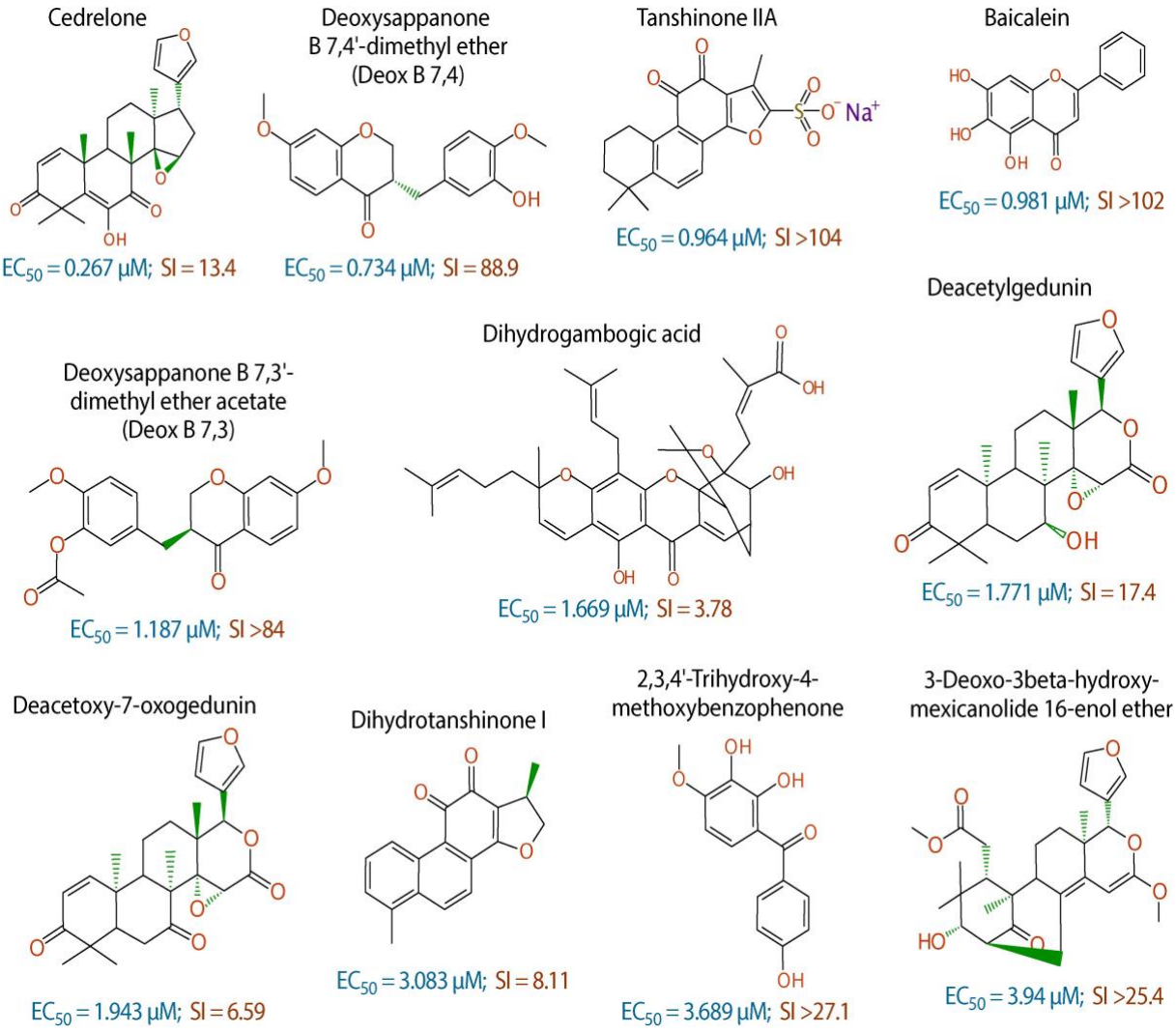
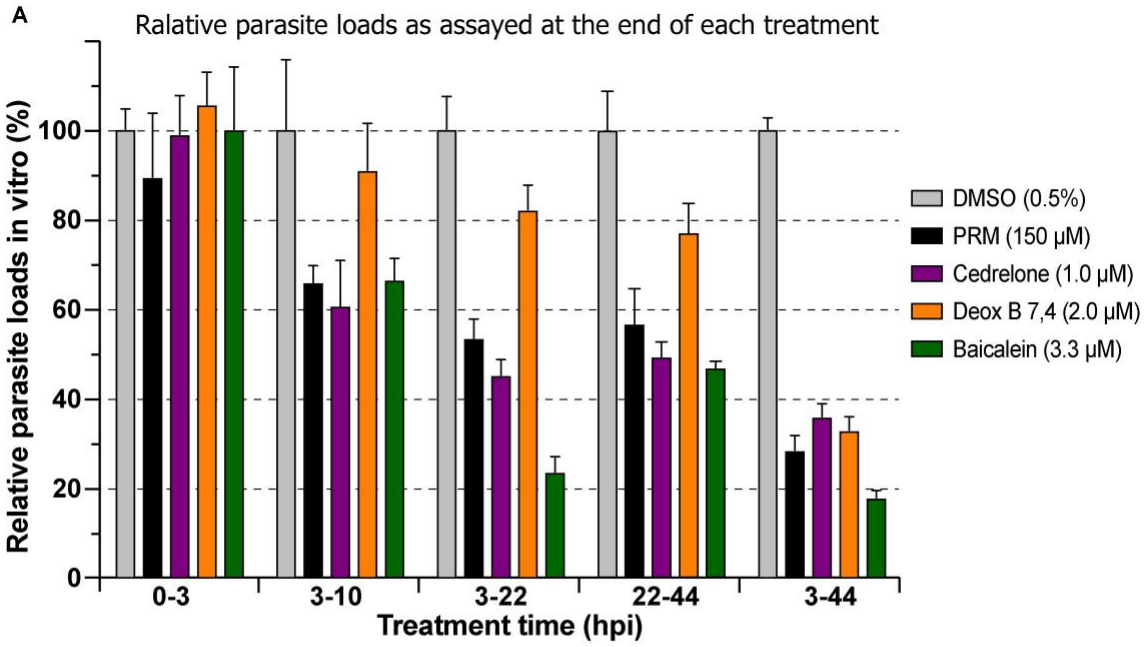



**Figure II-2 Chemical structures of the 11 top hits derived from plants and their in vitro $EC_{50}$ and safety interval (SI) values.**

### *2.3.2 Effect of cedrelone, Deox B 7,4 and baicalein on various parasite developmental stages*

Three of the top hits derived from plants were further evaluated for their effect on various developmental stages of *C. parvum* at around $EC_{60}$ to $EC_{80}$ concentrations (i.e., cedrelone at 1.0 μM, Deox B 7,4 at 2.0 μM and baicalein at 3.3 μM). All three compounds had no effect on the invasion of *C. parvum* sporozoites into host cells (**Fig. II-3**; 0-3 hpi treatment group). For intracellular parasites after 3 hpi, the levels of inhibition by the three compounds and paromomycin (PRM) control were generally correlated with the treatment length (**Figure II-3)**. However, for cedrelone or baicalein, a shorter treatment time (3 to 22 hpi group) could achieve a level of inhibition comparable to that of a full course of treatment (3-44 hpi group) (**Figure II-3)**, implying a relatively quick action of the two natural products on *C. parvum* in vitro. There were no highly significant differences between 3-22 hpi (earlier development) and 22-44 hpi (relatively later development) treatment groups for the three compounds.

A



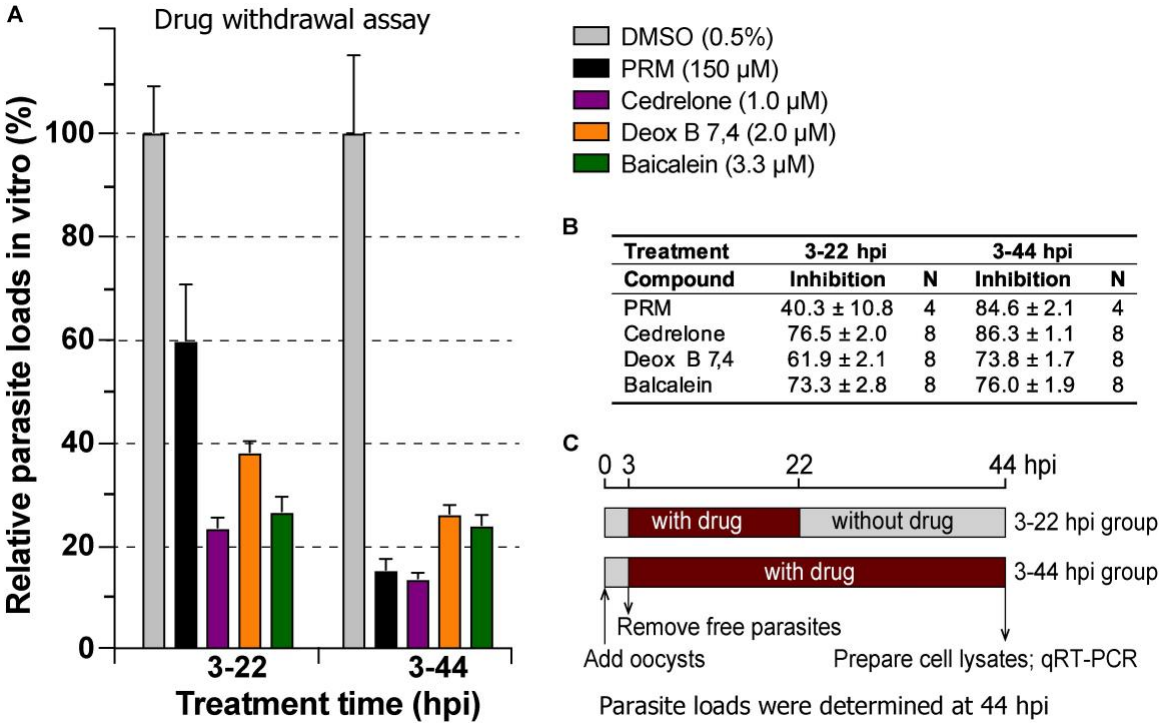

B Effect of compounds expressed as percent inhibition of the parasite growth

| Treatment | 0-3 hpi | | 3-10 hpi | | 3-22 hpi | | 22-44 hpi | | 3-44 hpi | |
|---|---|---|---|---|---|---|---|---|---|---|
| Compound | Inhibition (%) | N | Inhibition (%) | N | Inhibition (%) | N | Inhibition (%) | N | Inhibition (%) | N |
| PRM | 10.7 ± 14.2 | 8 | 34.2 ± 3.7 | 8 | 46.7 ± 4.3 | 8 | 43.4 ± 8.2 | 4 | 71.7 ± 3.3 | 8 |
| Cedrelone | 1.1 ± 8.7 | 8 | 39.5 ± 10.1 | 8 | 55.0 ± 3.5 | 8 | 50.7 ± 3.7 | 6 | 64.2 ± 2.9 | 8 |
| Deox B 7,4 | -5.5 ± 7.2 | 8 | 9.1 ± 10.4 | 8 | 18.0 ± 5.5 | 8 | 22.9 ± 6.8 | 8 | 67.2 ± 3.0 | 8 |
| Balcalein | 0 ± 13.9 | 6 | 33.7 ± 4.8 | 6 | 76.6 ± 3.4 | 6 | 53.1 ± 1.6 | 8 | 82.4 ± 1.6 | 6 |

**Figure II-3 Effects of cedrelone (1.0 µM), Deox B 7,4 (deoxysappanone B 7,4'-dimethyl ether) (2.0 µM) and baicalein (3.3 µM) on various developmental stage of *Cryptosporidium parvum* in vitro.**

**(A)** The effects were expressed as relative parasite loads in bar chart. **(B)** The effects were shown as percentage inhibitions on the parasite growth. The data included the effects on the excystation and invasion of sporozoites (0-3 hpi treatment group), early developmental stages representing first generation and some second generation of merogony (3-10 hpi and 3-22 hpi), and second generation of merogony and gametogenesis stage (22-44 hpi). Intracellular parasites receiving a full course of treatment were used for comparison (3-44 hpi). Diluent [dimethyl sulfoxide (DMSO) at 0.5%] only was used as a negative control. Paromomycin (PRM; 150 µM) was used as a positive control. In this assay, parasite loads were determined at the end of each treatment. hpi = hours post-infection time. Bars show the standard error of the mean (N = 6 or 8).

In drug withdrawal experiment suggested that the killing of the parasite by the three compounds were irreversible, because the parasites were unable to recover the growth well after being treated for 19 h (3-22 hpi treatment group) and allowed to growth without drugs for up to 44 hpi time point (vs. the 3-44 group receiving a full course of treatment) (**Figure II-4**). It was also noticeable that Deox B 7,4 acted on intracellular *C. parvum* differently from the other two compounds. When intracellular parasites received 3-22 hpi treatment with Deox B 7,4, the parasite loads were high when assayed at 22 hpi (i.e., 18.0% inhibition vs. 67.2% inhibition in 3-44 group in **Figure II-3**), but were unable to maintain growth after the removal of compound when assayed at 44 hpi (i.e., 61.9% inhibition vs. 73.8% inhibition in 3-44 group in **Figure II-4**). These observations suggested that Deox B 7,4 treatment produced a "delayed death effect" of intracellular *C. parvum* in vitro.




| Treatment | 3-22 hpi | | 3-44 hpi | |
|---|---|---|---|---|
| Compound | Inhibition | N | Inhibition | N |
| PRM | 40.3 ± 10.8 | 4 | 84.6 ± 2.1 | 4 |
| Cedrelone | 76.5 ± 2.0 | 8 | 86.3 ± 1.1 | 8 |
| Deox B 7,4 | 61.9 ± 2.1 | 8 | 73.8 ± 1.7 | 8 |
| Balcalein | 73.3 ± 2.8 | 8 | 76.0 ± 1.9 | 8 |

**Figure II-4 Drug withdrawal assay to evaluate the reversibility of the inhibition by cedrelone (1.0 µM), Deox B 7,4 (deoxysappanone B 7,4'-dimethyl ether) (2.0 µM) and baicalein (3.3 µM) on the growth of *Cryptosporidium parvum* in vitro.**
**(A)** Data were expressed as relative parasite loads in bar chart. **(B)** Data were shown as percentage inhibition on the parasite growth. **(C)** Illustration of the assay. In this assay, the parasites received treatments by individual compounds from 3 to 22 hpi time points, followed by the removal of compounds and continuous growth for up to 44 hpi time point. Intracellular parasites receiving a full course of treatment were used for comparison (3-44 hpi). Diluent (dimethyl sulfoxide at 0.5%) only was used as a negative control. Paromomycin (PRM; 150 µM) was used as a positive control. In this assay, parasite loads were determined at 44 hpi. Hpi = hours post-infection time. Bars show the standard error of the mean (N = 4 or 8).

## 2.4 Discussion

The present study represents the first large scale screening of natural products for discovering novel anti-cryptosporidial activity in vitro. By phenotypic screening of 800 natural products with defined structures (**Supplementary Tables A-1, A-2**), we identified 16 top hits showing low to sub-micromolar levels of activity against the growth of *C. parvum* in vitro (anti-cryptosporidial $EC_{50}$ values ranging from 0.122 to 3.940 μM). The 16 top hits represented compounds derived from microbes (n = 5) or plants (n = 11) (**Figure II-2** and **Table II-1**). Among microbial-derived compounds, in vitro anti-cryptosporidial activity of mitomycin and lovastatin was previously reported [114, 172, 173]. Daunorubicin was identified as one of the top hits against *C. parvum* in vitro in a recent phenotypic HTS of marketed drugs by us [116], although it was found earlier to be ineffective on cryptosporidial infection in rats [174]. The activity of valinomycin and dactinomycin against *Cryptosporidium* in vitro was previously unreported.

The remaining 11 compounds were phytochemicals from various plant species, for which their novel anti-cryptosporidial activities were observed for the first time. The most efficacious compound was cedrelone ($EC_{50}$ = 0.267 μM; SI = 13.4), which was a limonoid derived from the red cedar *Toona ciliate* or related species. Cedrelone was previously found to possess certain anti-microbial and in vitro anti-cancer activities [175-177], while no anti-parasitic activity was reported. The other three phytochemicals with sub-micromolar activity include: the homoisoflavanoid Deox B 7,4 ($EC_{50}$ = 0.734 μM) from heartwood of *Biancaea sappan* (syn. *Caesalpinia sappan*) known for anti-leukemic and anti-microtubule activity [178]; tanshinone IIA ($EC_{50}$ = 0.964 μM) as the main effective component of *Salvia miltiorrhiza* known as 'Danshen' in traditional Chinese medicine for treating cardiovascular disorders, as well as anti-

inflammatory/antioxidant activities [179]; and baicalein ($EC_{50}$ = 0.981 μM) from the root of *Scutellaria baicalensis* and *S. lateriflora* known as one of the active ingredients of Xiaochaihutang or Sho-Saiko-To, a Chinese herbal supplement believed to enhance liver health, as well as anti-cancer and anti-*Leishmania* activities [180-182].

Other phytochemicals were slightly less efficacious with anti-cryptosporidial $EC_{50}$ values ranging from 1.187 to 3.940 μM. Among them, Deox B 7,3, an anolog of Deox B 7,4, was previously identified as one of the inhibitors of cardiomyocyte hypertrophy [183]. Dihydrogambogic acid from a medical plant *Garcinia hanburyi* has been used topically to treat inflammatory skin disorders in China and found to be able to inhibit human matrix metalloproteinase 1 [184]. Deacetylgedunin is a limonoid (the 7-deacetyl derivative of gedunin) from *Azadirachta indica* known to possess anti-inflammatory and anti-malarial activities [185-188]. Deacetoxy-7-oxogedunin from *Carapa guianensis*, an analog of deacetylgedunin, was known for anti-malarial, hepatoprotective and collagen synthesis-promoting activities [188-192]. Dihydrotanshinone I is an analog of tanshinone IIA from *S. miltiorrhiza* with anti-cancer and anti-angiogenic activities [193, 194]. The final two compounds, 2,3,4'-trihydroxy-4-methoxybenzophenone (PubChem CID: 3908719) and 3-deoxo-3beta-hydroxymexicanolide 16-enol ether (CID: 6708594), were derivatives of natural products, for which significant biological activities have yet been reported.

At this stage of investigation, we were focusing on plant-derived compounds. Our further investigation of three top phytochemicals (i.e., cedrelone, Deox B 7,4 and baicalein) indicated that a relatively short time of treatment of all three compounds produced long-term inhibition on the intracellular parasites (i.e., irreversible killing) (**Figure II-4**). Among them, cedrelone and baicalein inhibited the parasite growth in a time-dependent manner, whereas Deox B 7,4

produced a “delayed death effect” on *C. parvum*. A “delayed death effect” was observed in other apicomplexan parasites when the replication of apicoplast organelles was inhibited [195-198]. In an earlier study on the anti-leukemic mechanism revealed that Deox B 7,4 was a reversible microtubule inhibitor that bound near the colchicine site, and could increase lysosomal V-ATPase activity and lysosome acidity in leukemia cells [178]. However, it still remains to be determined on whether the anti-cryptosporidial activity of Deox B 7,4 was attributed to its inhibition of the parasite microtubules. The Deox B 7,4-induced “delayed death effect” in *C. parvum* indicates that the pathway targeted by the compound is vital to the parasite, but it takes time to deplete its function after being inhibited by Deox B 7,4.

The discovery of new bioactive chemical scaffolds provides an opportunity for structure-activity relationship (SAR) to develop more effective and selective anti-cryptosporidial compounds. Using the top hit cedrelone as an example, although this compound is described as a derivative from the red cedar *T. ciliate*, its derivatives have been extracted from various plants, e.g., 9 and 10 cedrelone limonoids from *Walsura yunnanensis* and *Trichilia americana*, respectively [199, 200]. Using fingerprint Tanimoto-based 2-dimensional similarity search, we were also able to identify 215 compounds that shared $\geqslant$90% Tanimoto similarity with cedrelone from the PubChem database (https://pubchem.ncbi.nlm.nih.gov). It is noticeable that 4 of the 11 phytochemical top hits identified from 800 structurally diverse natural products are cedrelone limonoids, including cedrelone, 3-deoxo-3beta-hydroxymexicanolide 16-enol ether, deacetoxy-7-oxogedunin, and deacetylgedunin with structure similarity scores between 0.82792 and 0.83495 (vs. cedrelone) based on the Rubberbanding Forcefield similarity analysis implanted in DataWarrior version 5.0.0 [201]. Therefore, there are opportunities to acquire a sufficient number of cedrelone derivatives for subsequent SAR analysis. Similarly, derivatives of other top

hits are also available or extracted from plants in collaborating with experts in natural products for SAR analysis and discovery of new leads.

In summary, we have identified a significant number of natural products showing novel anti-cryptosporidial activities, in which detailed anti-parasitic efficacies in vitro, cytotoxicity and safety margins for 16 top hits were studied, together with more detailed analysis on the activity of three top phytochemicals. These findings, particularly the plant-derived natural products, provide us a large selection of new structures to be explored for developing anti-cryptosporidial therapeutics, such as further evaluating their efficacy in animal models, exploring their analogs for discovering more efficacious and safer inhibitors (hit-to-lead), and identifying their drug targets.

# CHAPTER III

# POTENTIAL SYNERGISTIC ANTI-CRYPTOSPORIDIAL ACTIVITY BY DRUG COMBINATIONS

## 3.1 Introduction

Cryptosporidiosis is an enteric disease caused by *Cryptosporidium spp.*, which are ubiquitous protozoan parasites and can infect virtually all vertebrates, including humans. The risk of this disease is greatly increased in immunocompromised patients, for which the symptoms can be protracted, severe or life-threatening. Although considerable efforts have been made to identify and develop new compounds with anti-cryptosporidial activity, effective therapy is yet unavailable for immunodeficient patients with cryptosporidiosis. Nitazoxanide (NTZ) as the only FDA-approved drugs for treating human cryptosporidiosis is partially effective in immunocompetent patients and ineffective in immunocompromised patients.

Systems biology has revealed that a disease is the result of disturbing complex networking systems with multiple signaling pathways [202-204]. Therefore, better effectiveness in treating a disease may be achieved through multi-intervention by multi-component therapies that simultaneously target different pathways. When two inhibitors are applied together, the combined effect may have the potential to achieve a greater efficacy than the sum of their individual potency (i.e., synergistic effect) [205, 206]. Given the potential benefits including increased efficacy, lowered toxicity and reduced adverse effects, drug combinations are being used as standard clinical options for treating cancers and many infectious diseases [144, 207-209].

In the past, the unappreciation of combinational therapy as therapeutic development in treating cryptosporidiosis, partly due to the limited availability of drugs. There were only very few reported studies exploring the combinations of drugs with known anti-cryptosporidial activities (e.g., NTZ, paromomycin, azithromycin, and rifabutin) [10, 92, 101, 210]. Currently, an increasing number of novel anti-cryptosporidial leads have been discovered recently [84, 116, 145, 210], which provides new opportunities to explore combinational therapeutic options against cryptosporidiosis. It now has the potential to become a new direction to explore and develop future therapeutic treatment.

This study aims to study the efficacy of combinations of selected compounds, including known anti-cryptosporidial drugs and newly discovered leads, to discover potential synergistic effects against *Cryptosporidium* in vitro serving as new options for developing treatments against cryptosporidiosis.

## 3.2 Materials and methods

### *3.2.1 In vitro culture of C. parvum*

The oocysts of *C. parvum* were acquired from Bunch Grass Farm (Deary, ID) and manipulated in vitro as described in Chapter II and in literature [108, 116]. The anti-cryptosporidial efficacies of selected compounds and their combination pairs were evaluated using a 44-h infection assay, which included 3 h of incubation of oocysts with host cell monolayers for excystation and invasion of sporozoites into host cells in the absence of drugs and subsequent 41 h intracellular development of the parasites in the presence of drugs. Cell lysates were prepared at 44 h post-infection (hpi) time point for qRT-PCR as described below.

### *3.2.2 qRT-PCR assay*

The qRT-PCR assay was performed to evaluate the parasite loads by detecting the levels of 18S rRNA transcripts (Cp18S) and host cell 18S rRNA transcripts (Hs18S) for normalization as described in Chapter 2 and literature [108]. Briefly, cells were lysed at 44 hpi time point by adding 150 µL ice-cold Bio-Rad iScript qRT-PCR sample preparation regent (lysis buffer) (Bio-Rad Laboratories, Hercules, CA) in each well, followed by the incubation at 75 ºC for 15 min, vortexing and centrifugation. Supernatants were collected and diluted, and qRT-PCR was performed by using a qScript one-step SYBR green qRT-PCR kit (Quanta Biosciences, Gaithersbury, MD) as described in Chapter 2

### *3.2.3 Anti-cryptosporidial compounds*

All compounds, including nitazoxanide (NTZ), paromomycin (PRM), vorinostat, paclitaxel, vatalanib, 2-deoxyglucose (2DG), gossypol, triacsin C were purchased from Sigma or as specified. These compounds were first prepared as a stock solution at 10 mM concentration according to the manufacturers' directions. They were selected based on their diverse targets in the parasite.

All experiments include at least two biological replicates for each combination in the *in vitro* treatment assay and two technical replicates for each biological replicate in the qRT-PCR assay.

### *3.2.4 Computation of drug combinational effects based on Bliss independence model*

Selected compounds were used to treat *C. parvum* cultured in vitro individually and in pairs at around $EC_{50}$ concentrations (half maximal effective to inhibit the parasite growth). For each pair of combination (e.g. drug **A** and drug **B**), we set 4 treatment groups, i.e., negative

control with diluent only (0.5% DMSO), drug **A** alone, drug **B** alone, and drugs **A** and **B** together. The inhibitory effects were evaluated via qRT-PCR method described above.

A Bliss independence model was used to evaluate the effective types of drug combinations [211], which assumed that the actions of individual compounds of a pair were independent events (additive effect). If drug **A** at concentration *a* inhibits $P_a$ percent of *C. parvum* growth and drug **B** at concentration *b* inhibits $P_b$ percent of parasite growth when they act alone, the percentage inhibition of combination $P_{ab,P}$ can be predicted by the complete additivity of probability theory using the following equation:

$$Pab,p\ (\%) = Pa + Pb - Pa \cdot Pb \qquad (3)$$

By comparison between the predicted level of inhibition (*Pab,p*) obtained in Eq. (3) and the actual level of inhibition observed in the in vitro assay (*Pab,o*), The effective types of drug combination could be interpreted as additive when $P_{ab,o} = P_{ab,p}$, synergistic when $P_{ab,o} > P_{ab,p}$ or antagonistic when $P_{ab,o} < P_{ab,p}$.

### 3.3 Results and discussion

We first selected 6 compounds for evaluating the combinational effect, including NTZ, PRM, vorinostat, vatalanib, paclitaxel and triacsin C. Among them, NTZ and PRM represent classic anti-cryptosporidial drugs known to target pyruvate:ferredoxin oxidoreductase and aminoacyl tRNA site of ribosomes, respectively [212, 213]. Vorinostat, vatalanib and paclitaxel were recently identified as some of the top lead compounds with anti-*Cryptosporidium* activity by screening 1200 marketed drugs, and known to target histone deacetylases, protein kinase and microtubules, individually [116]. Triacsin C was an anti-cryptosporidial lead targeting fatty acyl-CoA synthetase [84].

Anti-cryptosporidial efficacies were evaluated for the 6 compounds individually and in 9 drug pairs. Among the 9 drug pairs, the differences between observed inhibition and predicted inhibition ranged from -25.77% to 17.98% based on Bliss model (i.e., $\Delta P = P_{ab,o} - P_{ab,p}$,) (**Table III-1)**, indicating the presence of all three types of effects (i.e., antagonistic, additive and synergistic). For clarity, we classified antagonistic effect for drug pairs with $\Delta P < -10\%$, additive effect for pairs with $\Delta P$ from −10% and 10%, and synergistic effect for pairs with $\Delta P >$ 10%.

Among the 9 drug pairs, PRM paired with other compounds generally resulted in additive or synergistic effect ($\Delta P$ between −2.49% to −25.77%), whereas NTZ pairs generally resulted antagonistic effect ($\Delta P$ between 6.26% to 17.98%) (**Table III-1**). The "NTZ + vatalanib" pair gave the highest antagonistic effect, whereas the "PRM + triacsin C" gave the highest synergistic effect. These observations suggested that, among the two "classic" anti-cryptosporidial drugs, PRM is worth to be further explored for combinational therapy, whereas NTZ appeared to be unsuitable for developing combinational therapy.

**Table III-1 Observed and theoretical inhibition of compound combinations against the growth of *Cryptosporidium parvum* in vitro***

| Compound | Concentration (μM) | Observed Inhibition (%) | Predicted inhibition (%) | Observed minus Theoretical (%) | Note |
|---|---|---|---|---|---|
| Nitazoxanide (NTZ) | 4 | 42.21 | | | |
| Paromomycin (PRM) | 135 | 49.31 | | | |
| Paclitaxel | 0.099 | 69.96 | | | |
| Vorinostate | 0.203 | 43.12 | | | |
| Vatalanib | 0.322 | 39.90 | | | |
| Triacsin C | 0.5 | 48.75 | | | |
| NTZ + PRM | | 57.38 | 70.71 | -13.32 | Antagonistic |
| NTZ + Vatalanib | | 39.50 | 65.27 | -25.77 | Antagonistic |
| NTZ + Paclitaxel | | 77.05 | 82.64 | -5.58 | Additive |
| NTZ + Vorinostat | | 65.41 | 67.13 | -1.71 | Additive |
| NTZ + Triacsin C | | 67.89 | 70.38 | -2.49 | Additive |
| PRM + Vatalanib | | 85.21 | 69.54 | 15.67 | Synergistic |
| PRM + Paclitaxel | | 91.03 | 84.77 | 6.26 | Additive |
| PRM + Vorinostat | | 88.55 | 71.17 | 17.39 | Synergistic |
| PRM + Triacsin C | | 92.00 | 74.02 | 17.98 | Synergistic |

* Theoretical inhibitory activities were calculated under the assumption of additive effect of drug combinations.

Based the observation, the “PRM + vatalanib”, “PRM + vorinostat” and “PRM + triacsin C” pairs will be selected for further more detailed dose-response symmetry evaluation, where compounds at 3 concentrations (i.e., $EC_{25}$, $EC_{50}$ and $EC_{75}$ concentrations) are being used in various combinations as described in **Table III-1**. The dose symmetry study will provide information on the weight factor of individual drugs in contributing to the synergistic effect.

Combination of compounds other than NTZ and PRM (i.e., vorinostat, vatalanib, paclitaxel and triacsin C) are also being evaluated for discovering potential synergistic effect. These combinations will reveal the pathways to be targeted together for producing potential synergistic therapeutic values (e.g., chromatin modification, protein kinase, cytoskeleton and fatty acid metabolism).

Cytotoxicity (TC) of the best synergistic drug pairs will also be evaluated for calculating safety margins using an MTS assay as described in Chapter 2. The effect of drug combination will be similarly calculated according to the Bliss model based on predicted and observed TC values. The most desired combinations will be those showing the highest synergy in anti-cryptosporidial efficacy and highest antagonism in cytotoxicity.

In summary, we have evaluated 9 combinations of NTZ or PRM with other anti-cryptosporidial compounds and observed three drug pairs showing significant synergistic effect (i.e., “PRM + vatalanib”, “PRM + vorinostat” and “PRM + triacsin C” pairs) that were subjected to further investigation. These findings also indicated that synergy is achievable and combinational therapy is worth to be explored as an option in developing treatments against cryptosporidiosis.

# CHAPTER IV

# SUMMARY AND CONCLUSION

*Cryptosporidium* is a genus of parasitic protist in the Phylum Apicomplexa that infect virtually all vertebrate animals, including humans. Currently, at least 30 species have been reported [22, 113]. Among them, *C. parvum* and *C. hominis* are the two major species associated with human cryptosporidiosis [113, 214]. The parasite is mainly transmitted via fecal-oral route. Humans and animals may ingest the parasite oocysts that are resistant to disinfectants from drinking water, recreational water or food [215]. In humans, infected individuals may suffer symptoms e.g. watery diarrhea, abdominal pain, cramping and fever. Especially for individuals with compromised or weakened immunity, such as young children and AIDS patients, diarrhea can be chronic and severe, resulting in high morbidity and mortality [216, 217]. Therefore, *Cryptosporidium* parasites are considered as AIDS opportunistic pathogens and also classified as a Category B agent in the national biodefense program [218]. Cryptosporidiosis is also a significant health problem in animals. In farm animals, *Cryptosporidium* can cause neonatal diarrhea syndrome in calves, lambs and other young ruminants, resulting in considerable direct and indirect economic losses [13, 219, 220]. However, to date, nitazoxanide (NTZ) is the only drug approved by FDA for use in children over 1 year old and immunocompetent individuals, while only Halocur is approved for veterinary use in Canada and some other countries [221-223]. Therefore, there is an urgent need for developing novel anti-cryptosporidial therapeutics, particularly those for use in immunocompromised patients and livestock. As part of the drug discovery efforts, this study aimed to discover potential new anti-cryptosporidial therapeutic options.

In the discovery new anti-*Cryptosporidium* structures from natural products, we performed in vitro phenotypic high-throughput screening (HTS) of 800 natural products. In primary screening at 10 μM, 88 compounds were found to be able to inhibit the parasite growth by >60% and with low-to-moderate cytotoxicity. Secondary screening validated that 29 compounds retained >50% inhibition activity at 3.3 μM. Among them, 16 top hits exhibiting low to sub-micromolar activity against *C. parvum* growth were evaluated in more details, including determination of their $EC_{50}$ values (0.122 to 3.940 μM) and cytotoxicity $TC_{50}$ values (6.31 to >100 μM), in which 7 compounds had $EC_{50}$ values <1.0 μM.

Three compounds derived plants, including cedrelone (#3 hit; $EC_{50}$ = 0.267 μM), deoxysappanone b 7,4'-dimethyl ether (Deox B 7,4) (#5 hit; $EC_{50}$ = 0.734 μM), and baicalein (#7; $EC_{50}$ = 0.981 μM), were selected to further evaluated their efficacies on various parasite developmental stages in vitro at around $EC_{60}$ to $EC_{80}$ concentrations. The results showed that cedrelone and baicalein could could inhibit the parasite growth in a short period of time. Drug withdrawal assay further revealed that the three compounds could cause irreversible killing effect to parasite.

In the drug combination study, 6 compounds with known anti-cryptosporidial activity were selected for evaluating combinational effect, including NTZ, paromomycin (PRM), vorinostat, vatalanib, paclitaxel and triacsin C. Among the 9 drug combinations paired with NTZ or PRM, PRM paired with other compounds generally resulted in additive or synergistic effect, whereas NTZ pairs generally resulted antagonistic effect. The “NTZ + vatalanib” pair gave the highest antagonistic effect, whereas the “PRM + triacsin C” gave the highest synergistic effect. These observations suggested that, among the two “classic” anti-cryptosporidial drugs, PRM is

worth to be further explored for combinational therapy, whereas NTZ appeared to be unsuitable for developing combinational therapy.

In summary, we have discovered a set of new structures from natural products with excellent anti-cryptosporidial efficacies in vitro, which can be used for further drug design and development, such as evaluating their efficacy in animal models, exploring analogs for discovering more efficacious and safer inhibitors (hit-to-lead), and identifying their drug targets. We also identified that combination approaches as novel therapeutics options in against cryptosporidiosis in humans and animals. We also observed three drug pairs showing significant synergistic effect (i.e., “PRM + vatalanib”, “PRM + vorinostat” and “PRM + triacsin C”), indicating that synergy is achievable and combinational therapy is worth to be explored as an option in developing treatments against cryptosporidiosis.

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# APPENDIX

## SUPPLEMENTARY TABLE

**Table A-1 Primary screening at 10 µM: Anti-cryptosporidial activity shown as percent inhibition and cytotoxicity as evaluated by host cell Hs18S ΔCT values between treated and control groups. N/A: not applicable due to strong cytotoxicity.**

| # | Compound | CAS # | Formula | Mol Wt | Bioactivity and note | Plate # | Inhibition (%) | SEM | N | Hs18S $\Delta C_T$ | SEM | N | Cytotoxicity (%) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | DIGOXIN | 20830-75-5 | C41H64O14 | 780.96 | cardiac stimulant | p1 4-4 | NA | NA | NA | 14.32 | 0.10 | 2 | 100.0 |
| 2 | DIGITOXIN | 71-63-6 | C41H64O13 | 764.96 | inotropic, cardiotonic | p10 4-1 | NA | NA | NA | 13.47 | 0.04 | 4 | 100.0 |
| 3 | PROSCILLARIDIN | 466-06-8 | C29H40O9 | 532.64 | cardiotonic | p10 3-8 | NA | NA | NA | 13.28 | 0.08 | 4 | 100.0 |
| 4 | STROPHANTHIDIN | 66-28-4 | C23H32O6 | 404.51 | cardiotonic | p8 6-6 | NA | NA | NA | 11.98 | 0.27 | 4 | 100.0 |
| 5 | OUABAIN | 11018-89-6, 630-60-4 [anhydrous] | C29H44O12 | 584.67 | antiarrhythmic, cardiotonic, hypertensive, Na/K ATPase inhibitor | p10 9-4 | NA | NA | NA | 11.65 | 0.21 | 4 | 100.0 |
| 6 | DIHYDROCELASTRYL DIACETATE | 0 | C33H44O6 | 536.72 | chaperone stimulant | p3 6-4 | NA | NA | NA | 11.29 | 0.08 | 4 | 100.0 |
| 7 | CONVALLATOXIN | 508-75-8 | C29H42O10 | 550.65 | cardiotonic | p5 1-8 | NA | NA | NA | 10.84 | 0.08 | 4 | 99.9 |
| 8 | GAMBOGIC ACID | 2752-65-0 | C38H44O8 | 628.77 | antiinflammatory, cytotoxic, inhibits HeLa cells in vitro; | p4 8-7 | NA | NA | NA | 10.02 | 0.76 | 4 | 99.9 |
| 9 | PERUVOSIDE | 1182-67-2 | C30H44O9 | 548.68 | cardiotonic | p1 7-3 | NA | NA | NA | 10.85 | 0.13 | 4 | 99.9 |
| 10 | LANATOSIDE C | 17575-22-3 | C49H76O20 | 985.14 | cardiotonic | p8 2-2 | NA | NA | NA | 8.93 | 0.41 | 4 | 99.8 |
| 11 | GITOXIGENIN DIACETATE | 5996-03-2 | C27H38O7 | 474.60 | 0 | p4 9-3 | NA | NA | NA | 8.90 | 0.15 | 4 | 99.8 |
| 12 | CANTHARIDIN | 56-25-7 | C10H12O4 | 196.20 | irritant | p8 10-7 | NA | NA | NA | 7.39 | 0.40 | 4 | 99.4 |
| 13 | 3-OXOURSAN (28-13)OLIDE | 0 | C30H44O3 | 452.68 | 0 | p7 1-5 | NA | NA | NA | 6.62 | 0.62 | 4 | 99.0 |
| 14 | ANTHOTHECOL | 10410-83-0 | C28H32O7 | 480.56 | 0 | p4 1-5 | NA | NA | NA | 6.51 | 0.62 | 4 | 98.9 |
| 15 | POMIFERIN | 572-03-2 | C25H24O6 | 420.47 | antioxidant | p3 1-4 | NA | NA | NA | 6.42 | 0.06 | 4 | 98.8 |
| 16 | PODOFILOX | 518-28-5 | C22H22O8 | 414.42 | antineoplastic, inhibits microtubule assembly, and human DNA topoisomerase II; antimitotic agent | p7 5-1 | NA | NA | NA | 5.42 | 0.10 | 4 | 97.7 |
| 17 | 7-DESACETOXY-6,7-DEHYDROGEDUNIN | 0 | C26H30O5 | 422.53 | 0 | p4 5-1 | NA | NA | NA | 5.31 | 0.10 | 4 | 97.5 |
| 18 | ALPHA-MANGOSTIN | 6147-11-1 | C24H26O6 | 410.47 | 0 | p1 2-6 | NA | NA | NA | 4.36 | 0.14 | 4 | 95.1 |
| 19 | CELASTROL | 34157-83-0 | C29H38O4 | 450.62 | antineoplastic, NO synthesis inhibitor, chaperone stimulant | p2 5-2 | NA | NA | NA | 3.82 | 0.51 | 4 | 92.9 |
| 20 | 1,4,5,8-TETRAHYDROXY-2,6-DIMETHYLANTHROQUINONE | 19079-10-8 | C16H12O6 | 300.27 | 0 | p8 9-2 | NA | NA | NA | 3.65 | 1.94 | 4 | 92.0 |
| 21 | ESTRAGOLE | 140-67-0 | C10H12O | 148.21 | insect atttractant, skin irritant, carcinogen | p8 2-4 | 99.57 | 0.10 | 4 | -0.22 | 0.09 | 4 | -16.6 |
| 22 | CEDRELONE | 1254-85-9 | C26H30O5 | 422.53 | 0 | p1 6-1 | 99.50 | 0.02 | 4 | 1.38 | 0.14 | 4 | 61.7 |
| 23 | DIHYDROGAMBOGIC ACID | 0 | C38H46O8 | 630.79 | 0 | p1 4-3 | 97.74 | 0.05 | 4 | -0.60 | 0.38 | 4 | -52.0 |
| 24 | ABAMECTIN (AVERMECTIN B1A SHOWN) | 71751-41-2 | C48H72O14 | 873.10 | antiparisitic | p8 3-6 | 97.65 | 0.69 | 4 | 0.59 | 0.03 | 4 | 33.4 |
| 25 | AVERMECTIN A1A | 0 | C49H74O14 | 887.13 | antiparasitic | p5 1-7 | 97.32 | 0.18 | 4 | 0.02 | 0.06 | 4 | 1.6 |
| 26 | EMETINE DIHYDROCHLORIDE | 316-42-7, 483-18-1 [emetine] | C29H42Cl2N2O4 | 553.58 | inhibits RNA, DNA and protein synthesis | p2 1-4 | 97.26 | 0.12 | 4 | 1.41 | 0.13 | 4 | 62.4 |
| 27 | ISOOSAJIN | 5745-54-0 | C25H24O5 | 404.47 | 0 | p5 1-4 | 96.83 | 0.09 | 4 | -0.24 | 0.04 | 4 | -18.5 |
| 28 | STROPHANTHIDINIC ACID LACTONE ACETATE | 0 | C25H32O7 | 444.53 | 0 | p3 4-4 | 96.28 | 0.11 | 4 | 2.37 | 0.08 | 4 | 80.7 |
| 29 | HEXAMETHYLQUERCETAGETIN | 1251-84-9 | C21H22O8 | 402.40 | 0 | p3 1-7 | 95.76 | 0.38 | 4 | 1.01 | 1.12 | 4 | 50.3 |
| 30 | DIGOXIGENIN | 1672-46-4 | C23H34O5 | 390.52 | 0 | p3 6-5 | 95.61 | 0.22 | 4 | 0.33 | 0.15 | 4 | 19.2 |
| 31 | TRYPTAMINE | 61-54-1 | C10H12N2 | 160.22 | psychotropic | p8 7-2 | 95.48 | 0.27 | 4 | -0.43 | 0.14 | 4 | -34.7 |

| | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 32 | CAPREOMYCIN SULFATE | 1405-37-4, 11003-38-6 [capreomycin] | C25H46N14O12S | 766.80 | antibacterial, tuberculostatic | p7 2-8 | 95.26 | 0.39 | 4 | 0.30 | 0.07 | 4 | 18.5 |
| 33 | CRYPTOTANSHINONE | 35825-57-1 | C19H20O3 | 296.37 | inhibits angiogenesis | p4 2-8 | 95.26 | 0.39 | 4 | 0.18 | 0.07 | 4 | 11.9 |
| 34 | ACETYL ISOGAMBOGIC ACID | 0 | C40H46O9 | 670.81 | 0 | p3 7-5 | 95.25 | 0.23 | 4 | 1.57 | 0.05 | 4 | 66.4 |
| 35 | PLUMBAGIN | 481-42-5 | C11H8O3 | 188.18 | antibacterial, antifungal, tuberculostatic; antifeedant (worm) | p5 10-5 | 95.14 | 0.51 | 4 | 1.26 | 0.09 | 4 | 58.1 |
| 36 | PRISTIMERIN | 1258-84-0 | C30H40O4 | 464.65 | antineoplastic, antiinflammatory | p3 8-5 | 94.70 | 0.31 | 4 | 0.55 | 0.06 | 4 | 31.6 |
| 37 | ERYTHROMYCIN | 114-07-8 | C37H67NO13 | 733.95 | antibacterial | p6 2-8 | 94.62 | 0.66 | 4 | 0.62 | 0.11 | 4 | 35.0 |
| 38 | NOBILETIN | 478-01-3 | C21H22O8 | 402.40 | matrix metaloproteinase inhibitor; antineoplastic | p5 7-1 | 94.56 | 0.34 | 4 | 0.26 | 0.06 | 4 | 16.2 |
| 39 | DACTINOMYCIN | 50-76-0 | C62H86N12O16 | 1255.45 | antineoplastic, intercalating agent | p6 10-6 | 94.27 | 0.68 | 4 | 1.50 | 0.04 | 4 | 64.6 |
| 40 | MONENSIN SODIUM (MONENSIN A IS SHOWN) | 22373-78-0, 17090-79-8 (monensin) | C37H63NaO10 | 690.90 | antibacterial | p10 6-6 | 94.05 | 0.57 | 4 | 0.25 | 0.09 | 4 | 15.7 |
| 41 | MITOMYCIN | 50-07-7 | C15H18N4O5 | 334.33 | antineoplastic | p7 9-2 | 93.73 | 0.54 | 4 | 1.34 | 0.04 | 4 | 60.5 |
| 42 | SILIBININ | 22888-70-6 | C25H22O10 | 482.45 | hepatoprotective agent, antioxidant | p7 1-2 | 93.53 | 0.62 | 4 | -0.02 | 0.14 | 4 | -1.4 |
| 43 | RESVERATROL | 501-36-0 | C14H12O3 | 228.25 | antifungal, antibacterial | p4 1-2 | 93.53 | 0.62 | 4 | -0.13 | 0.14 | 4 | -9.6 |
| 44 | DIMETHYL GAMBOGINATE | 0 | C40H49ClO8 | 693.28 | 0 | p6 7-1 | 93.45 | 0.17 | 4 | 2.30 | 0.13 | 4 | 79.7 |
| 45 | HAEMATOPORPHYRIN | 14459-29-1 | C34H38N4O6 | 598.71 | antidepressant, antineoplastic | p8 9-4 | 93.06 | 0.57 | 4 | 1.45 | 1.28 | 4 | 63.3 |
| 46 | TOMATINE | 86273-92-9 | C47H79NO21 | 994.15 | antifungal, antibacterial, antiinflammatory agent | p9 3-6 | 92.89 | 0.17 | 4 | 0.04 | 0.04 | 4 | 2.7 |
| 47 | DIHYDROCELASTROL | 0 | C29H40O4 | 452.64 | 0 | p1 7-1 | 92.50 | 2.01 | 4 | 1.27 | 0.35 | 4 | 58.7 |
| 48 | 3-HYDROXYFLAVONE | 577-85-5 | C15H10O3 | 238.25 | 0 | p8 3-8 | 92.36 | 1.08 | 4 | -0.04 | 0.07 | 4 | -2.7 |
| 49 | VALINOMYCIN | 2001-95-8 | C54H90N6O18 | 1111.35 | antibiotic; LD50 (rat, po) 4 mg/kg | p7 4-1 | 92.27 | 0.83 | 4 | -0.13 | 0.06 | 4 | -9.2 |
| 50 | 3ALPHA-ACETOXYDIHYDRODEOXYGEDUNIN | 0 | C30H40O7 | 512.65 | 0 | p4 4-1 | 92.27 | 0.83 | 4 | -0.24 | 0.06 | 4 | -18.1 |
| 51 | RUTILANTINONE | 21288-61-9 | C22H20O9 | 428.40 | coccidiostat | p9 2-6 | 91.98 | 0.24 | 4 | -0.54 | 0.07 | 4 | -45.2 |
| 52 | BENZYL ISOTHIOCYANATE | 622-78-6 | C8H7NS | 149.22 | antineoplastic, antibacterial, antifungal | p9 1-8 | 91.81 | 0.55 | 4 | 0.57 | 0.09 | 4 | 32.8 |
| 53 | BETA-SITOSTEROL | 83-46-5 | C29H50O | 414.72 | 0 | p8 8-5 | 91.74 | 0.45 | 4 | 0.43 | 0.20 | 4 | 25.8 |
| 54 | URIDINE TRIPHOSPHATE TRISODIUM | 19817-92-6 | C9H12N2Na3O15P3 | 550.09 | psychostimulant | p8 2-1 | 91.48 | 2.02 | 4 | 0.23 | 0.14 | 4 | 14.5 |
| 55 | DEMETHYLNOBILETIN | 2174-59-6 | C20H20O8 | 388.38 | 0 | p1 6-8 | 91.41 | 1.46 | 4 | -0.06 | 0.08 | 4 | -4.6 |
| 56 | PATULIN | 149-29-1 | C7H6O4 | 154.12 | antibacterial | p9 10-4 | 91.38 | 0.40 | 4 | 0.81 | 0.10 | 4 | 43.0 |
| 57 | DEOXYSAPPANONE B 7,4'-DIMETHYL ETHER | 0 | C18H18O5 | 314.34 | 0 | p4 8-6 | 91.32 | 0.59 | 4 | 0.62 | 0.05 | 4 | 35.1 |
| 58 | LAPACHOL | 84-79-7 | C15H14O3 | 242.28 | antineoplastic, antifungal | p8 8-8 | 91.29 | 0.83 | 4 | -0.60 | 0.04 | 4 | -52.0 |
| 59 | DEACETYLGEDUNIN | 0 | C26H32O6 | 440.54 | 0 | p4 10-6 | 91.08 | 0.43 | 4 | 0.23 | 0.06 | 4 | 14.8 |
| 60 | CHRYSIN DIMETHYL ETHER | 21392-57-4 | C17H14O4 | 282.30 | 0 | p8 8-6 | 90.28 | 0.34 | 4 | -0.12 | 0.10 | 4 | -8.6 |
| 61 | 3-DEOXO-3BETA-HYDROXYMEXICANOLIDE 16-ENOL ETHER | 0 | C28H36O7 | 484.59 | 0 | P4 6-1 | 89.96 | 0.72 | 4 | -0.49 | 0.06 | 4 | -40.1 |
| 62 | 8BETA-HYDROXYCARAPIN, 3,8-HEMIACETAL | 0 | C27H32O8 | 484.55 | 0 | P3 5-7 | 89.65 | 0.47 | 4 | 0.18 | 0.09 | 4 | 11.8 |
| 63 | 5-HYDROXY-2',4',7,8-TETRAMETHOXYFLAVONE | 123316-61-0 | C19H18O7 | 358.35 | 0 | P6 5-7 | 89.23 | 0.31 | 4 | 0.20 | 0.05 | 4 | 13.2 |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 64 | DEACETOXY-7-OXOGEDUNIN | 0 | C26H30O6 | 438.53 | 0 | P3 8-8 | 88.69 | 1.41 | 4 | 0.39 | 0.09 | 4 | 23.6 |
| 65 | 3,16-DIDEOXYMEXICANOLIDE-3BETA-DIOL | 0 | C27H36O7 | 472.58 | 0 | P6 9-1 | 87.47 | 0.79 | 4 | -0.18 | 0.02 | 4 | -13.4 |
| 66 | DEOXYSAPPANONE B 7,3'-DIMETHYL ETHER ACETATE | 0 | C20H20O6 | 356.38 | 0 | P5 4-4 | 87.42 | 0.76 | 4 | 0.24 | 0.13 | 4 | 15.5 |
| 67 | OBTUSAQUINONE | 21105-15-7 | C16H14O3 | 254.29 | 0 | P4 6-5 | 87.13 | 1.25 | 4 | 0.84 | 0.05 | 4 | 44.3 |
| 68 | DIHYDROTANSHINONE I | 0 | C18H14O3 | 278.31 | 0 | P5 7-6 | 87.00 | 0.17 | 4 | 0.00 | 0.09 | 4 | 0.2 |
| 69 | RESERPINE | 50-55-5 | C33H40N2O9 | 608.69 | antihypertensive | P10 4-3 | 86.95 | 0.91 | 4 | 0.50 | 0.05 | 2 | 29.4 |
| 70 | ASARYLALDEHYDE | 4460-86-0 | C10H12O4 | 196.20 | fly attractant | P8 6-5 | 86.65 | 1.11 | 4 | -0.29 | 0.31 | 4 | -22.0 |
| 71 | PACLITAXEL | 33069-62-4 | C47H51NO14 | 853.93 | antineoplastic | p10 2-7 | 86.59 | 0.96 | 4 | 0.65 | 0.10 | 4 | 36.1 |
| 72 | CYCLOSPORINE | 59865-13-3 | C62H111N11O12 | 1202.64 | immunosuppressant | p10 2-6 | 86.52 | 0.40 | 4 | 0.16 | 0.04 | 4 | 10.4 |
| 73 | LOVASTATIN | 75330-75-5 | C24H36O5 | 404.55 | antihyperlipidemic, HMGCoA reductase inhibitor | p2 1-3 | 85.78 | 3.31 | 4 | 0.60 | 0.17 | 4 | 34.1 |
| 74 | 3-HYDROXYTYRAMINE | 62-31-7 | C8H11NO2 | 153.18 | dopaminergic | p1 9-6 | 85.53 | 0.92 | 4 | 0.76 | 0.23 | 4 | 41.1 |
| 75 | TRYPTOPHAN | 73-22-3 ['L'] | C11H12N2O2 | 204.23 | antidepressant, nutrient; LD50(rat) 1634 mg/kg ip | p1 7-6 | 85.53 | 0.92 | 4 | -0.75 | 0.11 | 3 | -68.2 |
| 76 | OCTOPAMINE HYDROCHLORIDE | 104-14-3 | C8H12ClNO2 | 189.64 | adrenergic agonist | p7 5-2 | 85.13 | 0.39 | 4 | -0.21 | 0.03 | 4 | -15.8 |
| 77 | BUSSEIN | 41060-14-4 | C43H54O18 | 858.90 | 0 | p4 5-2 | 85.13 | 0.39 | 4 | -0.33 | 0.03 | 4 | -25.3 |
| 78 | CYCLOVERATRYLENE | 0 | C27H30O6 | 450.54 | 0 | p8 1-5 | 83.81 | 2.02 | 4 | -0.03 | 0.07 | 4 | -2.2 |
| 79 | 2,3,4'-TRIHYDROXY-4-METHOXYBENZOPHENONE | 0 | C14H12O5 | 260.25 | 0 | p5 10-2 | 83.20 | 1.28 | 4 | 0.10 | 0.09 | 4 | 6.4 |
| 80 | 4-NONYLPHENOL | 104-40-5 | C15H24O | 220.36 | weevil pheromone, shows estrogenic activity | p9 9-8 | 83.12 | 1.61 | 4 | 0.14 | 0.09 | 4 | 9.2 |
| 81 | TANSHINONE IIA | 568-72-9 | C19H18O3 | 294.35 | antineoplastic, bone resorption inhibitor, antiproliferative, apoptosis inducer | p8 4-4 | 82.67 | 2.04 | 4 | 0.08 | 0.10 | 4 | 5.6 |
| 82 | HARMINE | 442-51-3 | C13H12N2O | 212.25 | antiparkinsonian, CNS stimulant | p9 4-8 | 82.22 | 1.87 | 4 | 0.49 | 0.07 | 4 | 28.6 |
| 83 | BAICALEIN | 491-67-8 | C15H10O5 | 270.24 | antiviral (HIV) | p3 3-3 | 81.26 | 1.15 | 4 | 0.10 | 0.07 | 4 | 6.7 |
| 84 | TETRANDRINE | 518-34-3 | C38H42N2O6 | 622.77 | analgesic, antineoplastic, antihypertensive, lymphotoxin | p9 1-7 | 80.44 | 0.57 | 4 | -0.04 | 0.02 | 4 | -2.5 |
| 85 | PICROPODOPHYLLIN | 477-47-4 | C22H22O8 | 414.42 | Insulin growth factor 1 receptor inhibitor, antineoplastic | p9 7-4 | 79.38 | 1.02 | 4 | 0.94 | 0.15 | 4 | 47.8 |
| 86 | IVERMECTIN | 70288-86-7 | C48H74O14 | 875.12 | antiparasitic | p10 1-8 | 78.97 | 1.16 | 4 | -0.05 | 0.08 | 4 | -3.4 |
| 87 | QUERCETIN | 117-39-5, 6151-25-3(hydrate) | C15H10O7 | 302.24 | capillary protectant, antioxidant. antineoplastic, anti-HIV | p7 7-4 | 78.42 | 1.12 | 4 | 0.34 | 0.03 | 4 | 21.1 |
| 88 | TETRAHYDROGAMBOGIC ACID | 0 | C38H48O8 | 632.80 | 0 | p9 2-8 | 77.89 | 0.85 | 4 | -0.31 | 0.12 | 4 | -23.6 |
| 89 | CHENODIOL | 474-25-9 | C24H40O4 | 392.58 | anticholithogenic, antilipemic agent | p10 5-5 | 77.73 | 5.03 | 4 | 0.27 | 0.09 | 2 | 17.2 |
| 90 | 3BETA-HYDROXYDEOXODIHYDRO DEOXYGEDUNIN | 0 | C28H38O6 | 470.61 | 0 | p4 7-4 | 77.26 | 1.07 | 4 | -0.26 | 0.11 | 4 | -19.7 |
| 91 | DAUNORUBICIN | 20830-81-3 | C27H29NO10 | 527.53 | antineoplastic | p10 2-1 | 76.78 | 6.50 | 4 | 0.99 | 0.18 | 4 | 49.5 |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 92 | SIROLIMUS | 53123-88-9 | C51H79NO13 | 914.20 | immunosuppressant, antineoplastic; rapamycin | p10 4-7 | 76.64 | 1.57 | 4 | 0.94 | 0.09 | 4 | 47.9 |
| 93 | SAFROLE | 94-59-7 | C10H10O2 | 162.19 | anesthetic (topical) and antiseptic, pediculicide | p9 3-8 | 76.16 | 2.02 | 4 | -0.44 | 0.12 | 4 | -35.3 |
| 94 | CAMPTOTHECIN | 7689-03-4 | C20H16N2O4 | 348.36 | antineoplastic | p5 5-7 | 75.97 | 3.37 | 4 | 1.35 | 0.01 | 4 | 60.8 |
| 95 | TACROLIMUS | 109581-93-3, 104987-11-3 [anhydrous] | C44H69NO12 | 804.04 | immune suppressant, antifungal | p10 3-7 | 75.57 | 1.18 | 4 | 0.16 | 0.03 | 4 | 10.4 |
| 96 | ROTENONE | 83-79-4 | C23H22O6 | 394.43 | acaricide, ectoparasiticide, antineoplastic, mitochondrial poison | p8 5-5 | 74.65 | 4.19 | 4 | 1.24 | 0.05 | 4 | 57.8 |
| 97 | PIPLARTINE | 20069-09-4 | C17H19NO5 | 317.34 | anti-asthma, antibronchitis | p5 5-1 | 73.69 | 1.52 | 4 | 0.33 | 0.09 | 4 | 20.5 |
| 98 | PODOPHYLLIN ACETATE | 1180-34-3 | C24H24O9 | 456.45 | 0 | p5 3-6 | 72.02 | 0.99 | 4 | 0.58 | 0.16 | 4 | 33.2 |
| 99 | VINBLASTINE SULFATE | 143-67-9, 865-21-4 [vinblastine] | C46H60N4O13S | 909.07 | antineoplastic, spindle poison | p6 2-7 | 71.70 | 1.71 | 4 | 0.81 | 0.14 | 4 | 43.0 |
| 100 | 1,3-DIDEACETYL-7-DEACETOXY-7-OXOKHIVORIN | 0 | C26H34O7 | 458.56 | 0 | p3 7-4 | 69.64 | 1.76 | 4 | 0.07 | 0.10 | 4 | 4.7 |
| 101 | QUINIC ACID | 77-95-2 | C7H12O6 | 192.17 | 0 | p7 6-8 | 69.36 | 1.31 | 4 | 0.23 | 0.06 | 4 | 14.6 |
| 102 | GLUTATHIONE | 70-18-8 | C10H17N3O6S | 307.33 | antioxidant | p9 5-8 | 68.08 | 1.20 | 4 | -0.40 | 0.05 | 4 | -32.0 |
| 103 | HESPERIDIN | 520-26-3 | C28H34O15 | 610.57 | capillary protectant | p7 7-8 | 66.25 | 1.79 | 4 | 0.35 | 0.05 | 4 | 21.5 |
| 104 | GRISEOFULVIN | 126-07-8 | C17H17ClO6 | 352.77 | antifungal, inhibits mitosis in metaphase | p10 6-8 | 66.05 | 4.17 | 4 | 0.30 | 0.06 | 4 | 18.7 |
| 105 | DIMETHYLSULFONE | 67-71-0 | C2H6O2S | 94.13 | antiinflammatory, antiproliferative, antiparasitic | p7 8-3 | 65.78 | 2.69 | 4 | 0.90 | 0.10 | 4 | 46.5 |
| 106 | STIGMASTA-4,22-DIEN-3-ONE | 20817-72-5 | C29H46O | 410.69 | 0 | p7 9-8 | 64.69 | 2.24 | 4 | 0.46 | 0.06 | 4 | 27.4 |
| 107 | MUNDULONE | 481-94-7 | C26H26O6 | 434.49 | 0 | p4 10-4 | 61.78 | 2.00 | 4 | 0.22 | 0.06 | 4 | 14.4 |
| 108 | DERRUSTONE | 2204-59-3 | C18H14O6 | 326.31 | 0 | p7 6-7 | 61.29 | 2.74 | 4 | 0.39 | 0.05 | 4 | 23.9 |
| 109 | LARIXINIC ACID | 118-71-8 | C6H6O3 | 126.11 | 0 | p7 8-8 | 59.78 | 3.35 | 4 | 0.20 | 0.11 | 4 | 12.9 |
| 110 | URSOCHOLANIC ACID | 546-18-9 | C24H40O2 | 360.59 | 0 | p9 1-1 | 59.28 | 3.21 | 4 | -0.10 | 0.02 | 4 | -6.9 |
| 111 | DESACETYL (7)KHIVORINIC ACID, METHYL ESTER | 0 | C28H40O10 | 536.63 | 0 | p8 10-5 | 58.59 | 1.85 | 4 | 0.00 | 0.51 | 4 | -0.1 |
| 112 | CIMICIFUGOSIDE H1 | 163046-73-9 | C35H52O9 | 616.80 | estrogen | p6 8-1 | 58.34 | 15.15 | 4 | 1.71 | 1.07 | 4 | 69.4 |
| 113 | ERYTHROSE | 583-50-6 | C4H8O4 | 120.11 | 0 | p7 10-8 | 57.20 | 0.97 | 4 | 0.23 | 0.09 | 4 | 14.6 |
| 114 | 1,2ALPHA-EPOXYDEACETOXYDIHYDROGEDUNIN | 0 | C26H32O7 | 456.54 | 0 | p5 10-1 | 56.48 | 4.23 | 4 | -0.18 | 0.06 | 4 | -12.9 |
| 115 | PAPAVERINE HYDROCHLORIDE | 61-25-6, 58-74-2 [papaverine] | C20H22ClNO4 | 375.86 | muscle relaxant (smooth), cerebral vasodilator | p10 5-8 | 56.16 | 1.09 | 4 | 0.57 | 0.08 | 4 | 32.7 |
| 116 | D-(+)-MALTOSE | 69-79-4 | C12H22O11 | 342.30 | nutrient, sweetener | p9 7-8 | 55.12 | 2.12 | 4 | -0.19 | 0.06 | 4 | -14.3 |
| 117 | RHOIFOLIN | 17306-46-6 | C27H30O14 | 578.53 | 0 | p9 1-6 | 54.61 | 3.06 | 4 | -0.26 | 0.04 | 4 | -20.0 |
| 118 | GARDENIN B | 2798-20-1 | C19H18O7 | 358.35 | 0 | p8 1-1 | 53.61 | 5.56 | 4 | 0.25 | 0.15 | 4 | 16.0 |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 119 | HEDERAGENIN | 465-99-6 | C30H48O4 | 472.71 | 0 | p1 1-7 | 53.42 | 2.88 | 4 | -0.11 | 0.17 | 4 | -7.7 |
| 120 | BLEOMYCIN (BLEOMYCIN B2 SHOWN) | 9041-93-4, 11056-06-7 [bleomycin] | C58H94N20O26S4 | 1615.77 | antineoplastic | p7 6-3 | 52.96 | 4.42 | 4 | -0.22 | 0.12 | 4 | -16.8 |
| 121 | ISOLIQUIRITIGENIN | 961-29-5 | C15H12O4 | 256.26 | aldose reductase inhibitor, antineoplastic, antiinflammatory | p9 2-7 | 52.92 | 4.21 | 4 | -0.34 | 0.10 | 4 | -26.4 |
| 122 | CANTHAXANTHIN (EUGLENANONE) | 514-78-3 | C40H52O2 | 564.86 | 0 | p9 3-7 | 52.72 | 2.15 | 4 | -0.26 | 0.05 | 4 | -19.8 |
| 123 | KHIVORIN | 2524-38-1 | C32H42O10 | 586.69 | 0 | p4 9-6 | 52.35 | 3.04 | 4 | 0.12 | 0.10 | 4 | 8.0 |
| 124 | EVERNINIC ACID | 570-10-5 | C9H10O4 | 182.18 | 0 | p9 8-8 | 52.13 | 4.07 | 4 | -0.34 | 0.06 | 4 | -26.6 |
| 125 | 3-HYDROXY-4-(SUCCIN-2-YL)-CARYOLANE DELTA-LACTONE | 0 | C19H28O4 | 320.43 | 0 | p7 7-7 | 51.45 | 0.73 | 4 | 0.49 | 0.04 | 4 | 28.8 |
| 126 | CASANTHRANOL [CASCAROSIDE A SHOWN] | 8024-48-4 | C21H22O10 | 434.40 | laxative, antineoplastic | p10 4-5 | 50.17 | 22.08 | 4 | 0.24 | 0.05 | 2 | 15.4 |
| 127 | BRUCINE | 4845-99-2, 357-57-3 [brucine] | C23H26N2O4 | 394.47 | central stimulant | p10 9-8 | 49.94 | 5.54 | 4 | -0.11 | 0.04 | 4 | -8.2 |
| 128 | 3,7-DIMETHOXYFLAVONE | 20950-52-1 | C17H14O4 | 282.30 | 0 | p8 9-6 | 49.73 | 2.16 | 4 | -0.21 | 0.13 | 4 | -15.4 |
| 129 | BIXIN | 39937-23-0 | C25H30O4 | 394.52 | 0 | p7 4-8 | 49.32 | 14.99 | 4 | 0.60 | 0.08 | 4 | 34.2 |
| 130 | 7,8-DIHYDROXYFLAVONE | 38183-03-8 | C15H10O4 | 254.24 | vascular protectant, antihaemorrhagic, tyr kinase B agonist | p4 4-8 | 49.32 | 14.99 | 4 | 0.49 | 0.08 | 4 | 28.8 |
| 131 | ETOPOSIDE | 33419-42-0 | C29H32O13 | 588.57 | antineoplastic | p7 7-3 | 48.52 | 0.42 | 4 | 0.40 | 0.06 | 4 | 24.1 |
| 132 | 18-AMINOABIETA-8,11,13-TRIENE SULFATE | 0 | C20H33NO4S | 383.55 | 0 | p9 6-7 | 47.65 | 5.55 | 4 | -0.19 | 0.04 | 4 | -13.9 |
| 133 | NARINGENIN | 480-41-1 | C15H12O5 | 272.26 | antiulcer, gibberellin antagonist | p9 6-1 | 47.57 | 4.37 | 4 | -0.23 | 0.12 | 4 | -17.3 |
| 134 | KASUGAMYCIN HYDROCHLORIDE | 19408-46-9, 6980-18-3 (base) | C14H26ClN3O9 | 415.83 | antifungal | p4 6-8 | 47.53 | 3.66 | 4 | -0.02 | 0.04 | 4 | -1.2 |
| 135 | SALSOLIDINE | 493-48-1 | C12H17NO2 | 207.27 | antihypertensive | p1 10-6 | 47.06 | 8.52 | 4 | 0.32 | 0.06 | 4 | 20.0 |
| 136 | BICUCULLINE (+) | 485-49-4 | C20H17NO6 | 367.36 | GABAa antagonist | p1 8-6 | 47.06 | 8.52 | 4 | -1.43 | 0.95 | 4 | -169.4 |
| 137 | 2-HYDROXY-5 (6)EPOXY-TETRAHYDROCARYOPHYLLENE | 0 | C15H26O2 | 238.37 | 0 | p3 2-8 | 46.23 | 2.96 | 4 | -0.15 | 0.08 | 4 | -10.9 |
| 138 | AVOCATIN A | 0 | C38H70O8 | 654.98 | antibacterial, antifungal | p7 5-6 | 46.03 | 5.16 | 4 | 0.00 | 0.04 | 4 | -0.1 |
| 139 | ENTANDROPHRAGMIN | 11013-05-1 | C43H56O17 | 844.92 | 0 | p4 5-6 | 46.03 | 5.16 | 4 | -0.12 | 0.04 | 4 | -8.3 |
| 140 | MUPIROCIN | 12650-69-0 | C26H44O9 | 500.64 | antibacterial, antimycoplasmal, isoleucyl-tRNA synthetase inhibitor | p10 4-8 | 45.65 | 1.20 | 4 | 0.09 | 0.08 | 4 | 5.8 |
| 141 | ASTAXANTHIN | 71772-51-5 | C40H52O4 | 596.86 | 0 | p1 4-1 | 45.11 | 4.28 | 4 | -0.43 | 0.18 | 4 | -34.8 |
| 142 | DEGUELIN(-) | 522-17-8 | C23H22O6 | 394.43 | antineoplastic, antiviral, insecticide | p3 5-5 | 45.04 | 6.26 | 4 | 0.60 | 0.30 | 4 | 34.2 |
| 143 | URIDINE | 58-96-8 | C9H12N2O6 | 244.21 | 0 | p5 7-8 | 44.81 | 4.43 | 4 | 0.02 | 0.08 | 4 | 1.4 |
| 144 | DEOXYADENOSINE | 16373-93-6 | C10H13N5O3 | 251.25 | 0 | p9 6-8 | 44.55 | 6.78 | 4 | -0.35 | 0.10 | 4 | -27.3 |
| 145 | 4'-METHOXYFLAVONE | 4143-74-2 | C16H12O3 | 252.27 | 0 | p9 6-3 | 44.41 | 2.12 | 4 | -0.09 | 0.22 | 4 | -6.3 |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 146 | MYCOPHENOLIC ACID | 24280-93-1 | C17H20O6 | 320.35 | immune suppressant, antineoplastic, antiviral | p10 8-4 | 44.40 | 4.30 | 4 | 1.03 | 0.08 | 4 | 51.1 |
| 147 | PIMPINELLIN | 131-12-4 | C13H10O5 | 246.22 | GABA receptor antagonist, phototoxin | p7 7-6 | 43.64 | 4.24 | 4 | 0.21 | 0.09 | 4 | 13.3 |
| 148 | AGELASINE (STEREOCHEMISTRY OF DITERPENE UNKNOWN) | 0 | C26H40ClN5 | 458.10 | cytotoxic, antineoplastic | p7 6-6 | 43.55 | 7.01 | 4 | 0.27 | 0.02 | 4 | 16.8 |
| 149 | SINENSETIN | 2306-27-6 | C20H20O7 | 372.38 | 0 | p3 9-6 | 42.77 | 3.36 | 4 | 0.39 | 0.05 | 4 | 23.6 |
| 150 | APRAMYCIN SULFATE | 65710-07-8 | C21H41N5O11 | 539.59 | antibacterial; LD50(iv) 280mg/kg(mouse) | p10 6-7 | 42.68 | 7.42 | 4 | -0.04 | 0.09 | 4 | -3.1 |
| 151 | COTININE | 486-56-6, 5695-98-7[fumarate] | C10H12N2O | 176.22 | antidepressant | P2 9-8 | 42.64 | 5.41 | 4 | 0.41 | 0.09 | 4 | 24.7 |
| 152 | CHOLIC ACID, METHYL ESTER | 1448-36-8 | C25H42O5 | 422.61 | 0 | p1 1-5 | 42.06 | 2.30 | 4 | -0.11 | 0.06 | 3 | -7.7 |
| 153 | LUPEOL | 545-47-1 | C30H50O | 426.73 | antineoplastic | p5 6-8 | 41.81 | 7.76 | 4 | 0.05 | 0.04 | 4 | 3.4 |
| 154 | BATYL ALCOHOL | 544-62-7 | C21H44O3 | 344.58 | 0 | p9 1-5 | 41.32 | 1.54 | 4 | -0.57 | 0.09 | 4 | -48.0 |
| 155 | MITRAPHYLLINE | 509-80-8 | C21H24N2O4 | 368.44 | antineoplastic | p5 9-8 | 41.31 | 4.01 | 4 | 0.17 | 0.16 | 4 | 11.1 |
| 156 | CARNOSINE | 305-84-0 | C9H14N4O3 | 226.24 | 0 | p4 8-8 | 41.12 | 2.69 | 4 | 0.08 | 0.13 | 4 | 5.5 |
| 157 | SISOMICIN SULFATE | 53179-09-2, 32385-11-8 [sisomicin] | C19H39N5O11S | 545.61 | antibacterial, binds to ribosomes | p10 5-3 | 41.06 | 26.87 | 4 | -0.11 | 0.09 | 2 | -7.8 |
| 158 | BOVINOCIDIN | 504-88-1 | C3H5NO4 | 119.08 | antineoplastic | p9 4-7 | 41.04 | 3.08 | 4 | -0.32 | 0.04 | 4 | -25.1 |
| 159 | 7-DEACETOXY-7-OXOKHIVORIN | 15004-51-0 | C30H38O9 | 542.63 | 0 | p3 9-8 | 40.16 | 1.36 | 4 | 0.21 | 0.06 | 4 | 13.5 |
| 160 | 6-HYDROXYFLAVONE | 6665-83-4 | C15H10O3 | 238.25 | 0 | p8 5-2 | 39.99 | 5.24 | 4 | 0.08 | 0.04 | 4 | 5.6 |
| 161 | CRUSTECDYSONE | 5289-74-7 | C27H44O7 | 480.65 | insect molting hormone | p9 5-7 | 39.83 | 0.40 | 4 | -0.15 | 0.03 | 4 | -10.6 |
| 162 | 6,7,2',3',4'-PENTAMETHOXYISOFLAVONE | 33978-66-4 | C20H20O7 | 372.38 | 0 | p2 6-4 | 39.55 | 3.29 | 4 | -0.38 | 0.31 | 4 | -30.1 |
| 163 | DAIDZEIN | 486-66-8 | C15H10O4 | 254.24 | phytoestrogen | p5 7-7 | 39.20 | 4.26 | 4 | 0.01 | 0.18 | 4 | 0.7 |
| 164 | PHENETHYLAMINE HYDROCHLORIDE | 156-28-5, 64-04-0 (base) | C8H12ClN | 157.64 | CNS stimulant | p8 10-2 | 39.04 | 2.69 | 4 | 2.99 | 2.02 | 4 | 87.4 |
| 165 | 2,3-DIHYDROXY-4-METHOXY-4'-ETHOXYBENZOPHENONE | 0 | C16H16O5 | 288.30 | 0 | p9 3-4 | 38.96 | 3.86 | 4 | -0.12 | 0.07 | 4 | -8.6 |
| 166 | L-DEOXYALLIIN | 21593-77-1 | C6H11NO2S | 161.22 | antineoplastic | p9 2-5 | 38.80 | 7.86 | 4 | -0.29 | 0.13 | 4 | -21.9 |
| 167 | ANDROGRAPHOLIDE | 5508-58-7 | C20H30O5 | 350.46 | antineoplastic | p5 4-5 | 38.80 | 1.92 | 4 | 0.08 | 0.02 | 4 | 5.3 |
| 168 | ACARBOSE | 56180-94-0 | C25H43NO18 | 645.62 | alpha-glucosidase & saccharase inhibitor, antidiabetes, antihyperlipidaemia, antiobesity | p10 5-7 | 37.83 | 2.12 | 4 | 0.39 | 0.04 | 4 | 23.6 |
| 169 | HUPERZINE A | 102518-79-6 | C15H18N2O | 242.32 | anticholinesterase, cognition enhancer | p3 4-8 | 37.59 | 7.61 | 4 | 0.19 | 0.15 | 4 | 12.4 |
| 170 | TUBOCURARINE CHLORIDE | 6989-98-6, 57-94-3 [anhydrous], 41354-45-4 [replaced], 57- | C37H42Cl2N2O6 | 681.66 | muscle relaxant (skeletal) | p10 10-8 | 37.53 | 2.58 | 4 | -0.29 | 0.13 | 4 | -22.2 |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | 95-4 [tubocurarine] | | | | | | | | | | | |
| 171 | GINKGOLIDE A | 15291-75-5 | C20H24O11 | 440.41 | antibacterial | p8 2-8 | 37.48 | 9.03 | 4 | 0.10 | 0.14 | 4 | 6.6 |
| 172 | ORSELLINIC ACID | 480-64-8 | C8H8O4 | 168.15 | 0 | p3 1-1 | 37.47 | 3.49 | 4 | -0.25 | 0.09 | 4 | -19.3 |
| 173 | ROSMARINIC ACID | 537-15-5 | C18H16O8 | 360.32 | antiinflammatory, antithrombotic, antiplatelet, cytostatic, antiviral | p3 1-5 | 37.27 | 1.47 | 4 | -0.04 | 0.23 | 4 | -3.1 |
| 174 | SALICIN | 138-52-3 | C13H18O7 | 286.28 | analgesic, antipyretic | p10 5-6 | 37.08 | 2.97 | 4 | 0.58 | 0.15 | 4 | 32.9 |
| 175 | BETULIN | 473-98-3 | C30H50O2 | 442.73 | 0 | p8 9-8 | 36.86 | 6.79 | 4 | -0.49 | 0.06 | 4 | -40.4 |
| 176 | UTILIN | 31218-22-1 | C41H52O17 | 816.86 | 0 | p3 10-8 | 36.84 | 1.74 | 4 | 0.06 | 0.09 | 4 | 4.2 |
| 177 | ALEURETIC ACID | 533-87-9 | C16H32O5 | 304.43 | 0 | p3 1-6 | 36.82 | 6.74 | 4 | 0.24 | 0.05 | 4 | 15.2 |
| 178 | NICOTINE BITARTRATE | 65-31-6 | C18H26N2O12 | 462.41 | nicotinyl acetylchloline receptor agonist, ectoparasiticide | p10 7-8 | 36.71 | 2.16 | 4 | -0.52 | 0.11 | 4 | -43.3 |
| 179 | CYTIDINE | 65-46-3 | C9H13N3O5 | 243.22 | 0 | p3 1-8 | 36.68 | 3.67 | 4 | -0.53 | 0.34 | 4 | -44.6 |
| 180 | DEOXYPEGANINE HYDROCHLORIDE | 61939-05-7 | C11H13ClN2 | 208.69 | acetylcholinesterase inhibitor, antiParkinsonism | p5 6-5 | 36.29 | 9.69 | 4 | -0.06 | 0.12 | 4 | -4.6 |
| 181 | HYOSCYAMINE | 101-31-5 | C17H23NO3 | 289.38 | anticholinergic, analgesic | p10 5-2 | 36.17 | 29.26 | 4 | -0.12 | 0.01 | 2 | -8.9 |
| 182 | BERGENIN | 477-90-7 | C14H16O9 | 328.28 | hepatoprotectant | P2 9-6 | 36.01 | 9.98 | 4 | 0.38 | 0.18 | 4 | 23.1 |
| 183 | GITOXIN | 4562-36-1 | C41H64O14 | 780.96 | cardiotonic | p1 3-5 | 35.41 | 4.02 | 2 | 0.08 | 0.04 | 2 | 5.4 |
| 184 | NYSTATIN | 114-90-9 | C47H75NO17 | 926.12 | antifungal, binds to membrane sterols | p10 4-4 | 34.97 | 20.87 | 4 | 1.05 | 0.58 | 4 | 51.7 |
| 185 | COLISTIN SULFATE | 1264-72-8 | C52H102N16O21S2 | 1351.62 | antibacterial | p10 10-7 | 33.43 | 13.56 | 4 | 0.01 | 0.05 | 4 | 0.4 |
| 186 | DIHYDROGEDUNIN | 0 | C28H36O7 | 484.59 | 0 | p3 7-8 | 33.28 | 4.27 | 4 | -0.24 | 0.04 | 4 | -17.9 |
| 187 | RETUSIN | 1245-15-4 | C19H18O7 | 358.35 | 0 | p9 10-5 | 33.24 | 4.57 | 4 | 0.27 | 0.06 | 4 | 17.0 |
| 188 | BETULINIC ACID | 472-15-1 | C29H46O3 | 442.69 | antineoplastic | p9 5-6 | 32.95 | 4.45 | 4 | -0.23 | 0.10 | 4 | -17.4 |
| 189 | DALBERGIONE | 0 | C15H12O2 | 224.26 | 0 | p5 9-3 | 32.77 | 5.71 | 4 | 0.33 | 0.07 | 4 | 20.4 |
| 190 | GIBBERELLIC ACID | 77-06-5 | C19H22O6 | 346.38 | 0 | p3 5-8 | 32.70 | 3.99 | 4 | 0.09 | 0.13 | 4 | 5.9 |
| 191 | MORIN | 480-16-0 | C15H10O7 | 302.24 | P450 and ATPase inhibitor | p4 7-8 | 32.34 | 4.90 | 4 | -0.21 | 0.04 | 4 | -15.6 |
| 192 | LACTOSE MONOHYDRATE | 62-42-3 | C12H24O12 | 360.32 | nutrient, pharmaceutic aid | p4 6-6 | 31.71 | 8.06 | 4 | 0.02 | 0.04 | 4 | 1.4 |
| 193 | MEXICANOLIDE | 1915-67-9 | C27H32O7 | 468.55 | 0 | p3 6-7 | 31.47 | 8.07 | 4 | -0.17 | 0.05 | 4 | -12.3 |
| 194 | MEPARTRICIN | 11121-32-7 | C60H88N2O19 | 1141.37 | antifungal, antiprotozoal | p7 2-1 | 31.44 | 5.64 | 4 | -0.51 | 0.08 | 4 | -42.4 |
| 195 | CARAPIN-8(9)-ENE | 0 | C27H30O7 | 466.54 | 0 | p4 2-1 | 31.44 | 5.64 | 4 | -0.62 | 0.08 | 4 | -54.0 |
| 196 | LARIXOL | 0 | C20H34O2 | 306.49 | 0 | p2 5-8 | 31.41 | 4.95 | 4 | 0.03 | 0.12 | 5 | 2.2 |
| 197 | DIHYDROGEDUNIC ACID, METHYL ESTER | 0 | C26H36O8 | 476.57 | 0 | p4 6-4 | 31.36 | 5.53 | 4 | -0.20 | 0.12 | 4 | -15.2 |
| 198 | SPAGLUMIC ACID | 4910-46-7 | C11H16N2O8 | 304.26 | neurotransmitter; mGluR3 receptors | p5 10-8 | 31.28 | 6.91 | 4 | 0.18 | 0.24 | 4 | 11.9 |
| 199 | ACTINONIN | 13434-13-4 | C19H35N3O5 | 385.51 | antibacterial | p5 4-8 | 31.27 | 4.56 | 4 | -0.06 | 0.04 | 4 | -4.6 |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 200 | 3-METHYLORSELLINIC ACID | 4707-46-4 | C9H10O4 | 182.18 | 0 | p4 6-7 | 30.83 | 3.87 | 4 | 0.05 | 0.03 | 4 | 3.6 |
| 201 | CARAPIN | 3463-88-5 | C27H32O7 | 468.55 | 0 | p3 6-8 | 30.71 | 8.06 | 4 | -0.07 | 0.10 | 4 | -5.2 |
| 202 | DALBERGIONE, 4-METHOXY-4'-HYDROXY- | 0 | C16H14O4 | 270.29 | 0 | p5 4-2 | 30.34 | 5.31 | 4 | 0.09 | 0.07 | 4 | 6.1 |
| 203 | PIPERONYLIC ACID | 94-53-1 | C8H6O4 | 166.13 | 0 | p3 2-7 | 30.30 | 3.46 | 4 | -0.04 | 0.10 | 4 | -3.1 |
| 204 | PACHYRRHIZIN | 10091-01-7 | C19H12O6 | 336.30 | insecticide | p3 2-1 | 29.77 | 5.27 | 4 | -0.08 | 0.10 | 4 | -6.0 |
| 205 | EPOXY (4,5alpha)-4,5-DIHYDROSANTONIN | 0 | C15H18O4 | 262.31 | 0 | P2 8-8 | 29.68 | 13.61 | 4 | -0.03 | 0.31 | 4 | -1.8 |
| 206 | PERILLYL ALCOHOL | 536-59-4, 18457-55-1 | C10H16O | 152.24 | antineoplastic, apoptosis inducer; skin irritant, LD50(rat) 2100 mg/kg po | p5 2-5 | 29.51 | 1.43 | 4 | -0.35 | 0.04 | 4 | -27.4 |
| 207 | QUASSIN | 76-78-8 | C22H28O6 | 388.46 | insecticide, antiamoebic | p7 5-8 | 29.35 | 5.75 | 4 | 0.08 | 0.10 | 4 | 5.1 |
| 208 | FERULIC ACID | 1135-24-6 | C10H10O4 | 194.19 | antineoplastic, choleretic, food preservative | p4 5-8 | 29.35 | 5.75 | 4 | -0.04 | 0.10 | 4 | -2.6 |
| 209 | KANAMYCIN A SULFATE | 25389-94-0, 133-92-6 [replaced], 59-01-8 [kanamycin] | C18H38N4O15S | 582.59 | antibacterial | p10 6-2 | 29.26 | 9.55 | 4 | -0.31 | 0.13 | 4 | -23.9 |
| 210 | EPOXYGEDUNIN | 0 | C28H34O8 | 498.58 | 0 | p5 2-4 | 29.04 | 3.64 | 4 | -0.46 | 0.08 | 4 | -37.3 |
| 211 | STRYCHNINE | 57-24-9 | C21H22N2O2 | 334.42 | central stimulant | p10 8-8 | 29.02 | 2.64 | 4 | -0.30 | 0.09 | 4 | -23.5 |
| 212 | PHLORIDZIN | 60-81-1 | C21H24O10 | 436.42 | induces experimental glucosuria, antifeedant | p7 1-7 | 28.85 | 5.29 | 4 | -0.08 | 0.02 | 4 | -5.8 |
| 213 | MENTHONE | 14073-97-3 | C10H18O | 154.25 | 0 | p4 1-7 | 28.85 | 5.29 | 4 | -0.20 | 0.02 | 4 | -14.5 |
| 214 | PUTRESCINE DIHYDROCHLORIDE | 0 | C4H14Cl2N2 | 161.08 | ornithine decarboxylase inhibitor, cell growth factor | p9 7-7 | 28.72 | 4.86 | 4 | -0.04 | 0.11 | 4 | -3.0 |
| 215 | DEOXYGEDUNIN | 21963-95-1 | C28H34O6 | 466.58 | neuroprotective, anti-depressant. learning enhancement | p2 5-1 | 28.62 | 9.62 | 4 | 0.24 | 0.09 | 4 | 15.4 |
| 216 | 6,4'-DIHYDROXYFLAVONE | 63046-09-3 | C15H10O4 | 254.24 | antihaemorrhagic | p9 8-1 | 28.18 | 11.52 | 4 | 0.28 | 0.14 | 4 | 17.9 |
| 217 | ESTRONE | 53-16-7 | C18H22O2 | 270.37 | estrogen | p10 9-1 | 28.09 | 4.10 | 4 | -0.24 | 0.05 | 4 | -18.4 |
| 218 | CADAVERINE TARTRATE | 462-94-2(base) | C7H16N2O6 | 224.22 | 0 | p4 9-8 | 27.52 | 5.85 | 4 | -0.06 | 0.05 | 4 | -4.5 |
| 219 | DEOXYKHIVORIN | 0 | C32H42O9 | 570.69 | 0 | p1 3-4 | 27.34 | 5.50 | 4 | 0.11 | 0.10 | 4 | 7.7 |
| 220 | 1,7-DIDEACETOXY-1,7-DIOXO-3-DEACETYLKHIVORIN | 0 | C26H32O7 | 456.54 | 0 | p4 8-1 | 26.84 | 3.45 | 4 | -0.10 | 0.04 | 4 | -6.9 |
| 221 | CHOLIC ACID | 81-25-4 | C24H40O5 | 408.58 | 0 | p1 1-6 | 26.71 | 2.48 | 4 | -0.40 | 0.03 | 4 | -32.0 |
| 222 | MEVALONIC ACID LACTONE | 503-48-0 | C6H10O3 | 130.14 | 0 | p7 10-7 | 26.69 | 3.56 | 4 | 0.26 | 0.07 | 4 | 16.5 |
| 223 | SCLAREOLIDE | 564-20-5 | C16H26O2 | 250.38 | antimicrobial | p1 1-1 | 26.58 | 5.98 | 4 | 0.57 | 0.18 | 4 | 32.7 |
| 224 | ADRENOLONE HYDROCHLORIDE | 62-13-5, 99-45-6 (base) | C9H12ClNO3 | 217.65 | adrenergic (opthalmic) | p6 8-8 | 26.43 | 5.66 | 4 | -0.22 | 0.02 | 4 | -16.6 |
| 225 | LIMONIN | 1180-71-8 | C26H30O8 | 470.52 | 0 | p7 1-8 | 26.18 | 5.78 | 4 | -0.12 | 0.05 | 4 | -8.4 |
| 226 | HECOGENIN | 467-55-0 | C27H42O4 | 430.63 | antiinflammatory | p4 1-8 | 26.18 | 5.78 | 4 | -0.23 | 0.05 | 4 | -17.3 |
| 227 | LUPININE | 486-70-4 | C10H19NO | 169.27 | antifeedant, antiinflammatory, oxytoxic | p3 2-4 | 26.07 | 3.70 | 4 | 0.18 | 0.12 | 4 | 11.8 |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 228 | VERATRINE SULFATE | 62-59-9 | C32H51NO13S | 689.83 | antihypertensive | p6 10-8 | 25.98 | 3.40 | 4 | -0.06 | 0.02 | 4 | -4.3 |
| 229 | LUPEOL ACETATE | 1617-68-1 | C32H52O2 | 468.77 | antiulcer | p5 6-7 | 25.85 | 8.48 | 4 | -0.17 | 0.06 | 4 | -12.1 |
| 230 | TYLOSIN TARTRATE | 1405-54-5, 1401-69-0(base) | C50H83NO23 | 1066.21 | antibacterial | p10 7-7 | 25.75 | 3.76 | 4 | -0.19 | 0.10 | 4 | -14.2 |
| 231 | ALLYLISOTHIOCYANATE | 57-06-7 | C4H5NS | 99.16 | counterirritant | p10 5-4 | 25.73 | 5.30 | 4 | 0.28 | 0.05 | 4 | 17.7 |
| 232 | THEAFLAVIN MONOGALLATES | 0 | C36H28O16 | 716.61 | 0 | p3 7-7 | 25.59 | 5.29 | 4 | -0.10 | 0.05 | 4 | -7.4 |
| 233 | SKATOLE | 83-34-1 | C9H9N | 131.18 | insect attractant | p7 8-7 | 25.24 | 4.65 | 4 | 0.30 | 0.04 | 4 | 18.5 |
| 234 | ASIATIC ACID | 464-92-6 | C30H48O5 | 488.71 | wound healing, experimental carcinogen | p5 6-1 | 25.12 | 1.68 | 4 | -0.29 | 0.09 | 4 | -22.7 |
| 235 | COLCHICINE | 64-86-8 | C22H25NO6 | 399.45 | antimitotic, antigout agent | p7 5-3 | 24.94 | 12.09 | 4 | -0.34 | 0.08 | 4 | -26.5 |
| 236 | OLEANOIC ACID | 508-02-1 | C30H48O3 | 456.72 | 0 | p4 5-3 | 24.94 | 12.09 | 4 | -0.45 | 0.08 | 4 | -36.8 |
| 237 | COLFORSIN | 66575-29-9 | C22H34O7 | 410.51 | adenylate cyclase activator, antiglaucoma, hypotensive, vasodilator | p10 1-7 | 24.79 | 7.28 | 4 | 0.14 | 0.05 | 4 | 9.4 |
| 238 | CHRYSANTHEMIC ACID, ETHYL ESTER | 0 | C12H20O2 | 196.29 | insecticide | p1 6-2 | 24.65 | 11.12 | 4 | -0.97 | 0.06 | 4 | -95.7 |
| 239 | METAMECONINE | 0 | C10H10O4 | 194.19 | 0 | p7 9-6 | 24.49 | 0.94 | 4 | 0.33 | 0.05 | 4 | 20.2 |
| 240 | BISANHYDRORUTILANTINONE | 749-18-8 | C22H16O7 | 392.37 | antibacterial | p9 7-6 | 24.47 | 2.89 | 4 | -0.16 | 0.11 | 4 | -12.0 |
| 241 | DOCOSANOL | 661-19-8 | C22H46O | 326.61 | antiviral | p6 1-8 | 24.37 | 1.69 | 4 | -0.38 | 0.06 | 4 | -30.5 |
| 242 | CURCUMIN | 458-37-7 | C21H20O6 | 368.39 | antiedemic, antiinflammatory, bile stimulant; antibacterial, antifungal, lipo/cyclooxygenase inhibitor | p3 7-6 | 24.26 | 5.24 | 4 | 0.03 | 0.02 | 4 | 2.4 |
| 243 | beta-CARYOPHYLLENE ALCOHOL | 0 | C15H26O | 222.37 | 0 | p3 3-8 | 24.19 | 6.28 | 4 | 0.03 | 0.04 | 4 | 1.9 |
| 244 | MEVASTATIN | 73573-88-3 | C23H34O5 | 390.52 | antihyperlipidemic, HMGCoA reductase inhibitor | p6 8-6 | 24.00 | 5.21 | 4 | 0.22 | 0.09 | 4 | 14.4 |
| 245 | SPERMIDINE TRIHYDROCHLORIDE | 0 | C7H22Cl3N3 | 254.63 | ornithine decarboxylase inhibitor | p8 7-1 | 23.90 | 2.28 | 4 | -0.63 | 0.05 | 4 | -54.4 |
| 246 | 3-NOR-3-OXOPANASINSAN-6-OL | 0 | C14H22O2 | 222.33 | 0 | p2 1-8 | 23.88 | 9.87 | 4 | 0.24 | 0.07 | 4 | 15.3 |
| 247 | 2-METHYLENE-5-(2,5-DIOXOTETRAHYDROFURAN-3-YL)-6-OXO--10,10-DIMETHYLBICYCLO[7: 2: 0]UNDECANE | 0 | C18H24O4 | 304.39 | 0 | p3 1-3 | 23.70 | 7.60 | 4 | -0.09 | 0.11 | 4 | -6.8 |
| 248 | AZADIRACHTIN | 11141-17-6 | C35H44O16 | 720.73 | antifeedant, insecticide | p7 1-6 | 23.68 | 7.08 | 4 | 0.00 | 0.03 | 4 | -0.1 |
| 249 | ORSELLINIC ACID, ETHYL ESTER | 2524-37-0 | C10H12O4 | 196.20 | 0 | p4 1-6 | 23.68 | 7.08 | 4 | -0.12 | 0.03 | 4 | -8.3 |
| 250 | METHYL GAMBOGATE METHYL ETHER | 0 | C40H48O8 | 656.82 | 0 | P2 7-6 | 23.61 | 5.17 | 4 | 0.37 | 0.20 | 4 | 22.4 |
| 251 | ADENOSINE PHOSPHATE | 61-19-8 | C10H14N5O7P | 347.23 | vasodilator, neuromodulator | p10 7-4 | 23.53 | 5.52 | 4 | -0.16 | 0.02 | 4 | -11.8 |
| 252 | METHYL DEOXYCHOLATE | 3245-38-3 | C25H42O4 | 406.61 | 0 | P2 10-7 | 23.38 | 14.27 | 4 | 0.66 | 0.07 | 4 | 36.7 |
| 253 | DJENKOLIC ACID | 498-59-9 | C7H14N2O4S2 | 254.33 | 0 | p3 3-1 | 23.33 | 8.14 | 4 | 0.00 | 0.05 | 4 | 0.2 |
| 254 | HYPOXANTHINE | 68-94-0 | C5H4N4O | 136.11 | 0 | p3 9-7 | 23.21 | 5.53 | 4 | 0.22 | 0.13 | 4 | 14.3 |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 255 | PICROTOXININ | 17617-45-7 | C15H16O6 | 292.29 | convulsant, GABA receptor antagonist, ichthyotoxin | p8 10-8 | 23.15 | 1.78 | 4 | -0.81 | 0.36 | 4 | -75.3 |
| 256 | DANTHRON | 117-10-2 | C14H8O4 | 240.22 | cathartic | p6 9-8 | 22.99 | 2.14 | 4 | -0.12 | 0.05 | 4 | -8.6 |
| 257 | RAUWOLSCINE HYDROCHLORIDE | 6211-32-1 | C21H27ClN2O3 | 390.91 | alpha2 adrenergic antagonist | p8 1-8 | 22.85 | 10.47 | 4 | -0.17 | 0.05 | 4 | -12.6 |
| 258 | XANTHOPTERIN | 119-44-8 | C6H5N5O2 | 179.14 | cell proliferation inhibitor | P2 10-2 | 22.72 | 5.69 | 4 | 0.47 | 0.20 | 4 | 27.9 |
| 259 | 2-ACETYLPYRROLE | 1072-83-9 | C6H7NO | 109.13 | hepatoprotectant, organoleptic | p9 2-4 | 22.62 | 11.65 | 4 | -0.43 | 0.13 | 4 | -34.6 |
| 260 | DEHYDROVARIABILIN | 0 | C17H14O4 | 282.30 | 0 | p2 4-5 | 22.03 | 3.24 | 4 | -0.42 | 0.13 | 4 | -33.6 |
| 261 | L(+/-)-ALLIIN | 556-27-4(-) | C6H11NO3S | 177.22 | antibacterial, antioxidant | p5 3-1 | 21.98 | 7.50 | 4 | -0.17 | 0.05 | 4 | -12.5 |
| 262 | ESTRADIOL | 50-28-2 | C18H24O2 | 272.39 | estrogen | p10 7-1 | 21.97 | 4.36 | 4 | -0.19 | 0.07 | 4 | -13.8 |
| 263 | NALOXONE HYDROCHLORIDE | 357-08-4, 51481-60-8 [dihydrate], 465-65-6 [naloxone] | C19H22ClNO4 | 363.84 | narcotic antagonist | p8 1-2 | 21.86 | 11.79 | 4 | 0.20 | 0.12 | 4 | 12.7 |
| 264 | LACCAIC ACID A | 15979-35-8 | C26H19NO12 | 537.44 | 0 | p3 2-6 | 21.81 | 2.10 | 4 | -0.09 | 0.06 | 4 | -6.6 |
| 265 | GOSSYPOL | 303-45-7 | C30H30O8 | 518.57 | antispermatogenic, antineoplastic, antiHIV | p9 7-5 | 21.38 | 3.16 | 4 | 0.45 | 0.05 | 4 | 26.6 |
| 266 | HYDROCORTISONE | 50-23-7 | C21H30O5 | 362.47 | glucocorticoid, antiinflammatory | p6 7-8 | 21.10 | 7.54 | 4 | -0.47 | 0.07 | 4 | -38.1 |
| 267 | CHOLINE CHLORIDE | 67-48-1, 62-49-7 [choline] | C5H14ClNO | 139.63 | choleretic, lipotropic, hepatoprotectant | p6 4-8 | 20.98 | 6.76 | 4 | 0.33 | 0.43 | 4 | 20.6 |
| 268 | PICROPODOPHYLLIN ACETATE | 0 | C24H24O9 | 456.45 | 0 | p8 8-1 | 20.82 | 8.69 | 4 | 1.02 | 0.05 | 4 | 50.6 |
| 269 | FRIEDELIN | 559-74-0 | C30H50O | 426.73 | 0 | p4 6-3 | 20.81 | 6.77 | 4 | -0.23 | 0.14 | 4 | -17.6 |
| 270 | CREATININE | 60-27-5 | C4H7N3O | 113.12 | metabolic enhancer | p5 6-6 | 20.47 | 12.29 | 4 | 0.00 | 0.03 | 4 | 0.2 |
| 271 | THEOPHYLLINE | 5967-84-0, 58-55-9 [anhydrous] | C7H8N4O2 | 180.17 | bronchodilator | p6 3-8 | 20.47 | 4.96 | 4 | -0.29 | 0.14 | 4 | -22.6 |
| 272 | CHRYSIN | 480-40-0 | C15H10O4 | 254.24 | diuretic | p4 7-7 | 20.34 | 2.92 | 4 | 0.14 | 0.02 | 4 | 9.3 |
| 273 | 2-METHOXYRESORCINOL | 29267-67-2 | C7H8O3 | 140.14 | 0 | p7 3-8 | 20.33 | 3.07 | 4 | -0.20 | 0.09 | 4 | -15.0 |
| 274 | XANTHURENIC ACID | 59-00-7 | C10H7NO4 | 205.17 | caspase activator, guanylyl cyclase stimulant | p4 3-8 | 20.33 | 3.07 | 4 | -0.32 | 0.09 | 4 | -24.4 |
| 275 | DEOXYSAPPANONE B TRIMETHYL ETHER | 0 | C19H20O5 | 328.37 | 0 | p5 3-4 | 20.25 | 5.01 | 4 | 0.04 | 0.07 | 4 | 2.4 |
| 276 | 4'-METHOXYCHALCONE | 22966-19-4 | C16H14O2 | 238.29 | 0 | p2 4-4 | 20.03 | 0.97 | 4 | -0.16 | 0.08 | 4 | -12.0 |
| 277 | BETAINE HYDROCHLORIDE | 590-46-5, 141-58-2 [replaced], 107-43-7 [betaine] | C5H12ClNO2 | 153.61 | antiarteriosclerotic, hypolipaemic, hepatoprotectant | p10 7-6 | 19.87 | 1.17 | 4 | -0.38 | 0.05 | 4 | -30.0 |
| 278 | KAEMPFEROL | 520-18-3 | C15H10O6 | 286.24 | 0 | p7 9-7 | 19.76 | 2.90 | 4 | 0.54 | 0.09 | 4 | 31.2 |
| 279 | PAROMOMYCIN SULFATE | 1263-89-4, 7542-37-2 [paromomycin], 59-04-1 | C23H47N5O18S | 713.72 | antibacterial, antiamebic | p10 9-6 | 19.72 | 5.12 | 4 | 0.08 | 0.05 | 4 | 5.5 |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | [paromomycin, replaced] | | | | | | | | | | | |
| 280 | DIALLYL SULFIDE | 592-88-1 | C6H10S | 114.21 | antibacterial, antifungal, antineoplastic, antihypercholesterolaemic, hepatoprotectant | p8 1-3 | 19.62 | 2.17 | 4 | -0.01 | 0.10 | 4 | -0.8 |
| 281 | 3-AMINO-beta-PINENE | 0 | C10H18ClN | 187.71 | 0 | p2 3-6 | 19.24 | 13.24 | 4 | 0.42 | 0.15 | 4 | 25.3 |
| 282 | EUPARIN | 532-48-9 | C13H12O3 | 216.24 | 0 | p2 5-6 | 19.01 | 4.38 | 4 | 0.23 | 0.06 | 4 | 14.6 |
| 283 | 2,6-DIHYDROXY-4-METHOXYTOLUENE | 0 | C8H10O3 | 154.17 | 0 | p9 7-1 | 18.96 | 8.38 | 4 | 0.06 | 0.12 | 4 | 4.4 |
| 284 | PEONOL METHYL ETHER | 829-20-9 | C10H12O3 | 180.21 | 0 | p9 4-6 | 18.92 | 6.94 | 4 | -0.31 | 0.17 | 4 | -24.3 |
| 285 | CAFFEIC ACID | 331-39-5 | C9H8O4 | 180.16 | 0 | p9 3-5 | 18.92 | 7.23 | 4 | -0.34 | 0.10 | 4 | -26.2 |
| 286 | USNIC ACID | 125-46-2 | C18H16O7 | 344.32 | antibacterial | p5 3-8 | 18.84 | 7.20 | 4 | -0.31 | 0.05 | 4 | -23.9 |
| 287 | TANGERITIN | 481-53-8 | C20H20O7 | 372.38 | 0 | p1 10-1 | 18.55 | 2.07 | 4 | 0.12 | 0.10 | 4 | 8.0 |
| 288 | SANGUINARINE SULFATE | 5578-73-4 | C20H15NO8S | 429.41 | antineoplastic, antiplaque agent | p1 8-1 | 18.55 | 2.07 | 4 | 0.07 | 0.04 | 4 | 4.9 |
| 289 | HELICIN | 618-65-5 | C13H16O7 | 284.27 | 0 | P2 10-8 | 18.55 | 13.31 | 4 | 0.07 | 0.11 | 4 | 4.7 |
| 290 | IZALPININ | 480-14-4 | C16H12O5 | 284.27 | 0 | p8 5-1 | 18.39 | 12.07 | 4 | 0.18 | 0.14 | 4 | 11.5 |
| 291 | LOBARIC ACID | 0 | C25H28O8 | 456.50 | 0 | p3 2-5 | 18.17 | 5.37 | 4 | 0.20 | 0.12 | 4 | 13.1 |
| 292 | DIHYDROSTREPTOMYCIN SULFATE | 5490-27-7, 128-46-1 [dihydrostreptomycin] | C21H43N7O16S | 681.68 | antibacterial, tuberculostatic | p10 5-1 | 17.98 | 8.83 | 4 | 0.05 | 0.21 | 4 | 3.4 |
| 293 | d,l-threo-3-HYDROXYASPARTIC ACID | 4294-45-5 | C4H7NO5 | 149.10 | L-aspartate beta-carboxylase inhibitor | p1 7-8 | 17.79 | 2.80 | 4 | 0.16 | 0.04 | 4 | 10.7 |
| 294 | HESPERETIN | 520-33-2 | C16H14O6 | 302.29 | 0 | p7 6-5 | 17.64 | 6.87 | 4 | -0.02 | 0.05 | 4 | -1.2 |
| 295 | OLEANDOMYCIN PHOSPHATE | 3922-90-5 (base) | C35H64NO16P | 785.87 | antibacterial | p6 6-8 | 17.62 | 4.33 | 4 | 3.02 | 3.38 | 4 | 87.6 |
| 296 | CATECHIN TETRAMETHYLETHER | 0 | C19H22O6 | 346.38 | 0 | p2 4-3 | 17.53 | 5.71 | 4 | -0.47 | 0.14 | 4 | -38.4 |
| 297 | CYANOCOBALAMIN | 68-19-9 | C63H92CoN14O14P | 1359.43 | vitamin, coenzyme B12 | p10 7-5 | 16.98 | 4.68 | 4 | -0.32 | 0.02 | 4 | -24.5 |
| 298 | CEPHARANTHINE | 481-49-2 | C37H38N2O6 | 606.73 | antineoplastic, hepatoprotectant, radiopropective | p6 9-6 | 16.84 | 14.23 | 4 | 0.33 | 0.09 | 4 | 20.5 |
| 299 | ARTEMISININ | 63968-64-9 | C15H22O5 | 282.34 | antimalarial | p5 8-8 | 16.73 | 3.78 | 4 | 0.00 | 0.04 | 4 | 0.0 |
| 300 | SALVINORIN A | 83729-01-5 | C23H28O8 | 432.47 | k-opiod receptor agonist, psychotropic | p7 3-5 | 16.71 | 5.50 | 4 | 0.53 | 0.09 | 4 | 30.5 |
| 301 | LEOIDIN | 105350-54-7 | C18H14Cl2O7 | 413.21 | 0 | p4 3-5 | 16.71 | 5.50 | 4 | 0.41 | 0.09 | 4 | 24.9 |
| 302 | EUCALYPTOL | 470-82-6 | C10H18O | 154.25 | anthelminthic, antiseptic, expectorant | p10 9-7 | 16.23 | 6.83 | 4 | -0.22 | 0.04 | 4 | -16.4 |
| 303 | 2-BENZOYL-5-METHOXYBENZOQUINONE | 0 | C14H10O4 | 242.23 | 0 | p5 1-1 | 16.19 | 4.32 | 4 | -0.59 | 0.02 | 4 | -50.7 |
| 304 | ARBUTIN | 497-76-7 | C12H16O7 | 272.26 | 0 | P2 9-3 | 16.10 | 4.42 | 4 | 0.01 | 0.09 | 4 | 0.5 |
| 305 | KAWAIN | 3155-48-4 | C14H14O3 | 230.27 | 0 | p7 1-4 | 15.98 | 3.82 | 4 | -0.15 | 0.07 | 4 | -10.9 |
| 306 | CYTISINE | 485-35-8 | C11H14N2O | 190.25 | antiinflammatory, respiratory stimulant | p4 1-4 | 15.98 | 3.82 | 4 | -0.26 | 0.07 | 4 | -20.0 |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 307 | PICEID METHYL ETHER | 30197-14-9 | C21H24O8 | 404.42 | antioxidant | p8 10-6 | 15.82 | 7.55 | 4 | 0.52 | 0.33 | 4 | 30.3 |
| 308 | AVOCADYNE ACETATE | 24607-06-5 | C19H34O4 | 326.48 | antifungal | p5 8-7 | 15.78 | 4.31 | 4 | 0.19 | 0.08 | 4 | 12.2 |
| 309 | 4-HYDROXY-6-METHYLPYRAN-2-ONE | 675-10-5 | C6H6O3 | 126.11 | 0 | p3 10-7 | 15.41 | 3.25 | 4 | 0.04 | 0.08 | 4 | 3.1 |
| 310 | TIGOGENIN | 77-60-1 | C27H44O3 | 416.65 | 0 | p2 4-7 | 15.39 | 2.37 | 4 | -0.40 | 0.02 | 4 | -31.8 |
| 311 | STREPTOMYCIN SULFATE | 3810-74-0, 57-92-1 [streptomycin] | C21H41N7O16S | 679.66 | antibacterial (tuberculostatic) | p10 7-3 | 15.36 | 5.64 | 4 | -0.10 | 0.04 | 4 | -7.1 |
| 312 | HAEMATOMMIC ACID, ETHYL ESTER | 39503-14-5 | C11H12O5 | 224.22 | 0 | P2 7-5 | 15.27 | 9.76 | 4 | 0.12 | 0.11 | 4 | 8.0 |
| 313 | SOLANESYL ACETATE | 0 | C47H76O2 | 673.13 | 0 | p4 6-2 | 15.24 | 4.90 | 4 | -0.20 | 0.10 | 4 | -14.8 |
| 314 | ANDROSTA-1,4-DIEN-3,17-DIONE | 897-06-3 | C19H24O2 | 284.40 | 0 | p3 6-6 | 15.07 | 12.25 | 4 | 0.01 | 0.11 | 4 | 0.7 |
| 315 | VISNAGIN | 82-57-5 | C13H10O4 | 230.22 | 0 | p1 1-2 | 15.05 | 13.87 | 3 | -0.27 | 0.17 | 4 | -20.7 |
| 316 | 2',4'-DIHYDROXY-4-METHOXYCHALCONE | 81674-91-1 | C16H14O4 | 270.29 | 0 | p1 4-2 | 14.88 | 10.99 | 4 | -1.00 | 0.20 | 4 | -99.8 |
| 317 | DERRUSNIN | 14736-62-0 | C19H16O7 | 356.34 | 0 | p7 2-7 | 14.81 | 6.25 | 4 | -0.10 | 0.12 | 4 | -7.3 |
| 318 | SALIDROSIDE | 10338-51-9 | C15H22O7 | 314.34 | 0 | p4 2-7 | 14.81 | 6.25 | 4 | -0.22 | 0.12 | 4 | -16.1 |
| 319 | DIOSGENIN | 512-04-9 | C27H42O3 | 414.63 | antiinflammatory, estrogen | p8 5-6 | 14.72 | 9.01 | 4 | 0.32 | 0.03 | 4 | 19.7 |
| 320 | ESTRIOL | 50-27-1, 514-68-1 [as, succinate] | C18H24O3 | 288.39 | estrogen | p10 8-1 | 14.41 | 3.17 | 4 | -0.12 | 0.03 | 4 | -8.4 |
| 321 | 1-MONOPALMITIN | 542-44-9 | C19H38O4 | 330.51 | 0 | p3 2-3 | 14.21 | 5.96 | 4 | -0.10 | 0.12 | 4 | -7.1 |
| 322 | URSINOIC ACID | 30265-59-9 | C15H16O5 | 276.29 | 0 | p6 1-3 | 14.19 | 6.68 | 4 | -0.46 | 0.15 | 4 | -37.5 |
| 323 | BIOCHANIN A | 491-80-5 | C16H12O5 | 284.27 | phytoestrogen | p7 7-5 | 14.14 | 1.37 | 4 | 0.10 | 0.06 | 4 | 6.9 |
| 324 | SCOPOLAMINE HYDROBROMIDE | 6533-68-2, 114-49-8 [anhydrous], 51-34-3 [scopolamine] | C17H22BrNO4 | 384.27 | anticholinergic, treatment of motion sickness | p8 10-1 | 13.97 | 3.61 | 4 | -0.37 | 0.08 | 4 | -29.6 |
| 325 | CHOLESTANE | 481-21-0 | C27H48 | 372.68 | 0 | p2 6-8 | 13.94 | 4.58 | 4 | 0.19 | 0.10 | 4 | 12.2 |
| 326 | EPIAFZELECHIN TRIMETHYL ETHER | 0 | C18H20O5 | 316.36 | 0 | p2 5-3 | 13.83 | 5.29 | 4 | 0.21 | 0.09 | 4 | 13.4 |
| 327 | DIOSMIN | 520-27-4 | C28H32O15 | 608.56 | vascular protectant | p5 2-1 | 13.82 | 8.13 | 4 | -0.65 | 0.08 | 4 | -57.1 |
| 328 | IRIGENIN TRIMETHYL ETHER | 0 | C21H22O8 | 402.40 | 0 | p5 1-3 | 13.72 | 5.05 | 4 | -0.48 | 0.11 | 4 | -39.9 |
| 329 | MUNDOSERONE | 3564-85-0 | C19H18O6 | 342.35 | 0 | p2 2-2 | 13.71 | 4.46 | 4 | 0.17 | 0.11 | 4 | 11.4 |
| 330 | COLCHICEINE | 477-27-0 | C21H23NO6 | 385.42 | antimitotic | p8 8-2 | 13.67 | 3.66 | 4 | -0.43 | 0.09 | 4 | -34.9 |
| 331 | SMILAGENIN | 126-18-1 | C27H44O3 | 416.65 | 0 | p2 3-1 | 13.52 | 9.54 | 4 | 0.58 | 0.17 | 4 | 33.2 |
| 332 | FORMONONETIN | 485-72-3 | C16H12O4 | 268.27 | phytoestrogen | p4 7-1 | 13.17 | 6.00 | 4 | -0.62 | 0.09 | 4 | -53.6 |
| 333 | 3,7-EPOXYCARYOPHYLLAN-6-ONE | 0 | C15H24O2 | 236.36 | 0 | p2 1-5 | 13.14 | 15.03 | 4 | 0.27 | 0.16 | 4 | 17.0 |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 334 | COUMARIN | 91-64-5 | C9H6O2 | 146.15 | antineoplastic, antiinflammatory, antihyperglycaemic | p6 4-1 | 12.97 | 3.50 | 4 | -0.05 | 0.05 | 4 | -3.8 |
| 335 | 2'-METHOXYFORMONETIN | 0 | C17H14O5 | 298.30 | 0 | p9 10-6 | 12.89 | 7.80 | 4 | 0.18 | 0.04 | 4 | 11.5 |
| 336 | 3,7-EPOXYCARYOPHYLLAN-6-OL | 0 | C15H26O2 | 238.37 | 0 | p2 6-5 | 12.87 | 11.01 | 4 | 0.11 | 0.02 | 4 | 7.2 |
| 337 | ASCORBIC ACID | 50-81-7 | C6H8O6 | 176.13 | antiscorbutic, antiviral | p10 3-6 | 12.01 | 3.61 | 4 | 0.44 | 0.46 | 4 | 26.2 |
| 338 | EPHEDRINE (1R,2S) HYDROCHLORIDE | 50-98-6, 299-42-3 [(-)-ephedrine] | C10H16ClNO | 201.70 | bronchodilator, cardiac stimulant | p8 4-1 | 11.97 | 8.77 | 4 | -0.06 | 0.14 | 4 | -4.2 |
| 339 | MONOCROTALINE | 315-22-0 | C16H23NO6 | 325.36 | antineoplastic, insect sterilant | p9 9-7 | 11.96 | 2.49 | 4 | 0.14 | 0.08 | 4 | 9.5 |
| 340 | ANHYDROBRAZILIC ACID | 0 | C12H10O5 | 234.21 | 0 | p4 7-6 | 11.90 | 1.58 | 4 | -0.01 | 0.07 | 4 | -0.5 |
| 341 | BIOTIN | 58-85-5 | C10H16N2O3S | 244.31 | vitamin B complex | p10 8-6 | 11.89 | 4.14 | 4 | -0.24 | 0.06 | 4 | -18.4 |
| 342 | INOSITOL | 87-89-8 | C6H12O6 | 180.16 | growth factor | p10 4-2 | 11.86 | 6.91 | 4 | 0.08 | 0.07 | 4 | 5.5 |
| 343 | ROTENONIC ACID, METHYL ETHER | 0 | C24H26O6 | 410.47 | 0 | p6 4-3 | 11.77 | 4.72 | 4 | 0.30 | 0.05 | 4 | 18.7 |
| 344 | 3,4-DIMETHOXYDALBERGIONE | 41043-20-3 | C17H16O4 | 284.31 | induces dermatitis | p8 3-7 | 11.56 | 11.82 | 4 | 0.06 | 0.04 | 4 | 3.8 |
| 345 | HARMALOL HYDROCHLORIDE DIHYDRATE | 6028-07-5 | C12H17ClN2O3 | 272.73 | anthelmintic, narcotic agent | p8 7-8 | 11.47 | 5.47 | 4 | -0.76 | 0.07 | 4 | -69.6 |
| 346 | PERSEITOL | 527-06-0 | C7H16O7 | 212.20 | 0 | p2 4-2 | 11.32 | 4.16 | 4 | -0.23 | 0.23 | 4 | -17.1 |
| 347 | beta-AMYRIN ACETATE | 1616-93-9 | C32H52O2 | 468.77 | 0 | p5 8-4 | 11.26 | 3.57 | 4 | 0.01 | 0.06 | 4 | 0.5 |
| 348 | QUINIDINE GLUCONATE | 7054-25-3, 6591-63-5 [quinidine sulfate], 56-54-2 [quinidine] | C26H36N2O9 | 520.58 | antiarrhythmic, antimalarial | p10 2-3 | 11.23 | 4.82 | 4 | -0.03 | 0.08 | 4 | -2.0 |
| 349 | SAPPANONE A DIMETHYL ETHER | 0 | C18H16O5 | 312.33 | 0 | p5 4-3 | 11.12 | 6.11 | 4 | 0.18 | 0.06 | 4 | 11.8 |
| 350 | ANTIMYCIN A (A1 shown) | 1397-94-0 | C27H38N2O9 | 534.61 | antifungal, antiviral, interferes in cytochrome oxidation | p5 4-7 | 10.91 | 5.69 | 4 | 0.12 | 0.15 | 4 | 7.7 |
| 351 | 11a-ACETOXYPROGESTERONE | 2268-98-6 | C23H32O4 | 372.51 | metabolite of progesterone | p5 4-1 | 10.83 | 5.10 | 4 | -0.22 | 0.08 | 4 | -16.6 |
| 352 | CATECHIN PENTAACETATE | 0 | C25H24O11 | 500.46 | 0 | p9 6-6 | 10.66 | 6.03 | 4 | -0.26 | 0.03 | 4 | -19.6 |
| 353 | ESCULIN MONOHYDRATE | 531-75-9 | C15H18O10 | 358.30 | antiinflammatory | p8 9-7 | 10.62 | 2.38 | 4 | -0.42 | 0.12 | 4 | -34.0 |
| 354 | LUPANINE PERCHLORATE | 550-90-3 (base) | C15H25ClN2O5 | 348.83 | 0 | p1 9-2 | 10.49 | 11.23 | 4 | -0.09 | 0.03 | 4 | -6.1 |
| 355 | DIHYDROROTENONE | 0 | C23H24O6 | 396.44 | 0 | p8 10-3 | 10.36 | 5.33 | 4 | 0.76 | 0.10 | 4 | 40.9 |
| 356 | SHIKIMIC ACID | 138-59-0 | C7H10O5 | 174.15 | 0 | p1 7-2 | 10.28 | 12.75 | 4 | 0.06 | 0.15 | 4 | 3.9 |
| 357 | THEAFLAVIN | 4670-05-7 | C29H24O12 | 564.51 | antioxidant | p4 8-5 | 10.19 | 1.90 | 4 | 0.11 | 0.06 | 4 | 7.6 |
| 358 | SEROTONIN HYDROCHLORIDE | 50-67-9 | C10H13ClN2O | 212.68 | neurotransmitter | p3 6-1 | 10.18 | 7.38 | 4 | -0.40 | 0.05 | 4 | -31.7 |
| 359 | HEMATEIN | 475-25-2 | C16H12O6 | 300.27 | 0 | p1 9-3 | 10.13 | 3.46 | 4 | 0.13 | 0.03 | 4 | 8.6 |
| 360 | EPIGALLOCATECHIN-3-MONOGALLATE | 989-51-5 | C22H18O11 | 458.38 | 0 | p2 6-3 | 10.02 | 3.33 | 4 | -0.19 | 0.24 | 4 | -14.2 |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 361 | TETRAHYDROSAPPANONE A TRIMETHYL ETHER | 0 | C19H22O5 | 330.38 | 0 | p8 2-5 | 9.90 | 14.12 | 4 | -0.10 | 0.10 | 4 | -6.9 |
| 362 | 4'-HYDROXYCHALCONE | 2657-25-2 | C15H12O2 | 224.26 | 0 | P2 8-6 | 9.45 | 17.15 | 4 | 0.33 | 0.24 | 4 | 20.5 |
| 363 | SANTONIN | 481-06-1 | C15H18O3 | 246.31 | 0 | P2 10-3 | 9.41 | 6.60 | 4 | 0.18 | 0.08 | 4 | 11.8 |
| 364 | CEDRYL ACETATE | 77-54-3 | C17H28O2 | 264.41 | 0 | p2 5-7 | 9.38 | 7.19 | 4 | 0.05 | 0.26 | 4 | 3.6 |
| 365 | PALMATINE CHLORIDE | 10605-02-4 | C21H22ClNO4 | 387.87 | antibacterial, antimalarial, uterine contractant | p3 8-4 | 9.29 | 3.91 | 4 | -0.09 | 0.06 | 4 | -6.1 |
| 366 | 7-HYDROXYFLAVONE | 6665-86-7 | C15H10O3 | 238.25 | antifungal, analgesic | p7 3-6 | 9.24 | 3.62 | 4 | 0.17 | 0.05 | 4 | 10.8 |
| 367 | SECURININE | 5610-40-2 | C13H15NO2 | 217.27 | GABAA receptor blocker, CNS stimulant | p4 3-6 | 9.24 | 3.62 | 4 | 0.05 | 0.05 | 4 | 3.6 |
| 368 | LAGOCHILIN | 23554-81-6 | C20H36O5 | 356.51 | 0 | P2 7-1 | 9.20 | 3.84 | 4 | 0.60 | 0.13 | 4 | 34.1 |
| 369 | ROBUSTIC ACID | 5307-59-5 | C22H20O6 | 380.40 | 0 | p5 9-7 | 9.13 | 7.61 | 4 | 0.28 | 0.10 | 4 | 17.8 |
| 370 | PHENACYLAMINE HYDROCHLORIDE | 5468-37-1, 613-89-8(base) | C8H10ClNO | 171.63 | 0 | p8 10-4 | 9.11 | 3.46 | 4 | 1.22 | 0.29 | 4 | 57.0 |
| 371 | OROTIC ACID | 65-86-1 | C5H4N2O4 | 156.10 | hepatoprotectant, uricosuric agent | p6 6-5 | 8.85 | 2.92 | 4 | -0.39 | 0.14 | 4 | -31.1 |
| 372 | ANABASAMINE HYDROCHLORIDE | 20410-87-1(base) | C16H20ClN3 | 289.81 | 0 | P2 8-1 | 8.75 | 22.46 | 4 | 0.40 | 0.11 | 4 | 24.3 |
| 373 | FARNESOL | 4602-84-0 | C15H26O | 222.37 | 0 | p5 8-6 | 8.75 | 3.76 | 4 | 0.02 | 0.03 | 4 | 1.0 |
| 374 | ARABITOL | 7643-75-6 | C5H12O5 | 152.15 | 0 | p2 5-4 | 8.73 | 8.93 | 4 | -0.04 | 0.10 | 4 | -2.6 |
| 375 | CITRININ | 518-75-2 | C13H14O5 | 250.25 | antibacterial | p1 3-7 | 8.51 | 0.32 | 2 | 0.13 | 0.11 | 2 | 8.3 |
| 376 | ANTIAROL | 642-71-7 | C9H12O4 | 184.19 | 0 | p4 7-5 | 8.48 | 1.70 | 4 | 0.10 | 0.04 | 4 | 6.9 |
| 377 | ARISTOLOCHIC ACID | 313-67-7 | C17H11NO7 | 341.28 | PLA2 inhibitor | p9 6-2 | 8.39 | 7.27 | 4 | -0.03 | 0.24 | 4 | -1.8 |
| 378 | HYDROLYSIS PRODUCT OF BUSSEIN | 0 | C32H40O14 | 648.67 | 0 | p2 4-8 | 8.30 | 8.98 | 4 | -0.69 | 0.03 | 4 | -60.9 |
| 379 | DEHYDROABIETAMIDE | 0 | C20H29NO | 299.46 | 0 | p7 2-5 | 8.30 | 1.98 | 4 | -0.01 | 0.04 | 4 | -0.7 |
| 380 | BRAZILIN | 474-07-7 | C16H14O5 | 286.29 | 0 | p4 2-5 | 8.30 | 1.98 | 4 | -0.12 | 0.04 | 4 | -8.9 |
| 381 | ONONETIN | 487-49-0 | C15H14O4 | 258.28 | 0 | p9 7-2 | 8.27 | 4.90 | 4 | -0.18 | 0.11 | 4 | -12.9 |
| 382 | ALLANTOIN | 97-59-6 | C4H6N4O3 | 158.12 | wound healing agent | p10 1-5 | 8.13 | 3.78 | 4 | -0.22 | 0.14 | 4 | -16.1 |
| 383 | 2-HYDROXY-3,4-DIMETHOXYBENZOIC ACID | 5653-46-3 | C9H10O5 | 198.18 | prostaglandin synthetase inhibitor | p7 4-7 | 7.69 | 4.70 | 4 | 0.16 | 0.07 | 4 | 10.5 |
| 384 | 3-DESHYDROXYSAPPANOL TRIMETHYL ETHER | 0 | C19H22O5 | 330.38 | 0 | p4 4-7 | 7.69 | 4.70 | 4 | 0.05 | 0.07 | 4 | 3.2 |
| 385 | TRETINOIN | 302-79-4 | C20H28O2 | 300.44 | keratolytic, antiacne, antineoplastic | p10 2-8 | 7.49 | 5.74 | 4 | -0.28 | 0.02 | 4 | -21.5 |
| 386 | SCLAREOL | 515-03-7 | C20H36O2 | 308.51 | antineoplastic, apoptosis inducer | p6 1-6 | 7.29 | 10.13 | 4 | -0.15 | 0.05 | 4 | -10.7 |
| 387 | DEHYDROEPIANDROSTERONE | 53-43-0 | C19H28O2 | 288.43 | 0 | p4 10-8 | 7.05 | 3.42 | 4 | -0.03 | 0.06 | 4 | -1.9 |
| 388 | EPIGALLOCATECHIN | 970-74-1 | C15H14O7 | 306.27 | 0 | p2 5-5 | 7.01 | 3.36 | 4 | 0.15 | 0.06 | 4 | 9.9 |
| 389 | ANABASINE HYDROCHLORIDE | 13078-04-1 (anabasine) | C10H15ClN2 | 198.70 | insecticide | p3 8-7 | 6.88 | 6.75 | 4 | -0.08 | 0.11 | 4 | -5.5 |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 390 | BERBAMINE HYDROCHLORIDE | 478-61-5 (berbamine) | C37H42Cl2N2O6 | 681.66 | antihypertensive, skeletal muscle relaxant | p8 6-8 | 6.86 | 18.93 | 4 | -0.21 | 0.12 | 4 | -15.6 |
| 391 | GENISTEIN | 446-72-0 | C15H10O5 | 270.24 | increases bone mineral density | p6 3-3 | 6.85 | 14.63 | 4 | 0.20 | 0.01 | 4 | 12.7 |
| 392 | 3beta-HYDROXYISOALLOSPIROST-9(11)-ENE | 0 | C27H42O3 | 414.63 | 0 | p6 7-7 | 6.79 | 10.10 | 4 | -0.17 | 0.06 | 4 | -12.6 |
| 393 | RETINOL | 68-26-8 | C20H30O | 286.46 | vitamin A | p10 1-6 | 6.73 | 3.26 | 4 | 0.09 | 0.07 | 4 | 6.3 |
| 394 | AZELAIC ACID | 123-99-9 | C9H16O4 | 188.23 | antiacne, antiproliferative agent | p10 3-4 | 6.72 | 8.45 | 4 | 0.03 | 0.05 | 4 | 1.8 |
| 395 | HECOGENIN ACETATE | 915-35-5 | C29H44O5 | 472.67 | 0 | p1 9-5 | 6.66 | 5.55 | 4 | -0.05 | 0.08 | 4 | -3.7 |
| 396 | FUCOSTANOL | 83-45-4 | C29H52O | 416.74 | 0 | p1 7-5 | 6.66 | 5.55 | 4 | -0.69 | 0.15 | 4 | -61.6 |
| 397 | GEDUNIN | 2753-30-2 | C28H34O7 | 482.58 | antifeedant; heat shock inducer | p8 7-6 | 6.58 | 8.52 | 4 | 0.02 | 0.03 | 4 | 1.2 |
| 398 | EPICATECHIN MONOGALLATE | 1257-08-5 | C22H18O10 | 442.38 | 0 | p2 3-3 | 6.24 | 5.97 | 4 | 0.38 | 0.08 | 4 | 23.1 |
| 399 | LINAMARIN | 554-35-8 | C10H17NO6 | 247.25 | 0 | p1 6-6 | 6.23 | 7.26 | 4 | 0.59 | 0.08 | 4 | 33.5 |
| 400 | ADONITOL | 488-81-3 | C5H12O5 | 152.15 | 0 | P2 7-4 | 6.19 | 1.71 | 4 | 0.26 | 0.11 | 4 | 16.4 |
| 401 | 2',4'-DIHYDROXYCHALCONE | 1776-30-3 | C15H12O3 | 240.26 | anthelmintic, antiulcer | p7 2-6 | 6.05 | 1.97 | 4 | 0.09 | 0.10 | 4 | 6.1 |
| 402 | KOPARIN | 65048-75-1 | C16H12O6 | 300.27 | 0 | p4 2-6 | 6.05 | 1.97 | 4 | -0.02 | 0.10 | 4 | -1.6 |
| 403 | HOMOPTEROCARPIN | 606-91-7 | C17H16O4 | 284.31 | 0 | p3 3-5 | 5.57 | 3.90 | 4 | -0.01 | 0.09 | 4 | -0.7 |
| 404 | ANISODAMINE HYDROBROMIDE | 17659-49-3 | C17H23NO4 | 305.38 | anticholinergic, antispasmodic | p5 1-2 | 5.51 | 11.32 | 4 | -0.41 | 0.17 | 4 | -32.6 |
| 405 | YOHIMBINE HYDROCHLORIDE | 65-19-0 | C21H27ClN2O3 | 390.91 | alpha adrenergic blocker, mydriatic, antidepressant | p10 6-4 | 5.49 | 13.70 | 4 | -0.45 | 0.07 | 4 | -36.5 |
| 406 | LUPANYL ACID HYDROCHLORIDE | 0 | C14H25ClN2O2 | 288.82 | 0 | p5 7-5 | 5.40 | 7.81 | 4 | 0.09 | 0.15 | 4 | 6.0 |
| 407 | CYSTAMINE DIHYDROCHLORIDE | 56-17-7 | C4H14Cl2N2S2 | 225.20 | hepatoprotectant, radioprotectant | p6 6-6 | 5.08 | 1.87 | 4 | -0.15 | 0.05 | 4 | -11.2 |
| 408 | GARLICIN | 2179-57-9 | C6H10S2 | 146.27 | antineoplastic, antibacterial, apoptosis inducer, insecticide | p5 1-6 | 4.93 | 13.44 | 4 | -0.39 | 0.07 | 4 | -30.8 |
| 409 | GLUCITOL-4-GUCOPYANOSIDE | 0 | C12H24O11 | 344.32 | 0 | p9 4-5 | 4.89 | 7.96 | 4 | -0.19 | 0.06 | 4 | -14.4 |
| 410 | AVOCATIN B | 0 | C34H66O6 | 570.90 | 0 | p7 10-5 | 4.87 | 5.74 | 4 | 0.36 | 0.07 | 4 | 21.9 |
| 411 | DIHYDROFISSINOLIDE | 0 | C29H38O8 | 514.62 | 0 | p4 9-2 | 4.50 | 2.93 | 4 | 0.08 | 0.05 | 4 | 5.3 |
| 412 | OMEGA-3-ACID ESTERS (EPA shown) | 86227-47-6 | C22H34O2 | 330.52 | hypolipidemic | p6 1-7 | 4.36 | 14.00 | 4 | -0.23 | 0.06 | 4 | -17.4 |
| 413 | DIHYDROMUNDULETONE | 0 | C25H28O6 | 424.50 | 0 | p2 6-7 | 4.35 | 5.15 | 4 | -0.10 | 0.03 | 4 | -7.4 |
| 414 | BEKANAMYCIN SULFATE | 4696-76-8 (base) | C18H39N5O14S | 581.60 | antibacterial | p10 3-5 | 4.16 | 9.06 | 4 | 0.13 | 0.07 | 4 | 8.7 |
| 415 | PICEID | 27208-80-6 | C20H22O8 | 390.39 | antioxidant | p5 2-7 | 4.10 | 0.69 | 4 | -0.36 | 0.13 | 4 | -28.7 |
| 416 | TOBRAMYCIN | 32986-56-4 | C18H37N5O9 | 467.52 | antibacterial, inhibits protein synthesis | p10 9-3 | 4.08 | 4.67 | 4 | -0.49 | 0.19 | 4 | -40.8 |
| 417 | GRAYANOTOXIN I | 4720-09-6 | C22H36O7 | 412.53 | 0 | p1 1-3 | 3.95 | 7.58 | 4 | -0.03 | 0.26 | 3 | -2.4 |
| 418 | CAFFEINE | 58-08-2, 5743-12-4 [monohydrate | C8H10N4O2 | 194.19 | CNS stimulant | p2 1-1 | 3.94 | 4.95 | 4 | 0.27 | 0.08 | 4 | 16.9 |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 419 | AURAPTENE | 495-02-3 | C19H22O3 | 298.39 | antineoplastic, apoptosis inducer | p5 9-1 | 3.93 | 6.03 | 4 | 0.02 | 0.12 | 4 | 1.2 |
| 420 | ACTEIN | 18642-44-9 | C37H56O11 | 676.85 | antihypertensive | p8 9-1 | 3.90 | 15.38 | 4 | -0.41 | 0.09 | 4 | -33.3 |
| 421 | QUERCITRIN | 522-12-3 | C21H20O11 | 448.39 | antihemmorrhagic | p2 2-1 | 3.89 | 5.08 | 4 | -0.65 | 0.46 | 4 | -57.2 |
| 422 | CINCHONIDINE | 485-71-2 | C19H22N2O | 294.40 | antimalarial | p8 4-7 | 3.76 | 12.00 | 4 | -0.20 | 0.06 | 4 | -15.2 |
| 423 | ATROPINE SULFATE | 51-55-8, 5908-99-6 [atropine sulfate], 55-48-1 [anhydrous] | C17H25NO7S | 387.46 | anticholinergic, mydriatic | P2 9-1 | 3.70 | 7.88 | 4 | 0.26 | 0.03 | 4 | 16.3 |
| 424 | FOLIC ACID | 59-30-3 | C19H19N7O6 | 441.41 | hematopoietic vitamin | p6 8-7 | 3.63 | 3.37 | 4 | 0.02 | 0.05 | 4 | 1.3 |
| 425 | SYRINGIC ACID | 530-57-4 | C9H10O5 | 198.18 | 0 | p3 8-1 | 3.63 | 5.94 | 4 | -0.26 | 0.07 | 4 | -20.0 |
| 426 | THYMOQUINONE | 0 | C10H12O2 | 164.21 | 0 | p8 1-4 | 3.13 | 18.98 | 4 | -0.08 | 0.07 | 4 | -5.8 |
| 427 | EUGENOL | 97-53-0 | C10H12O2 | 164.21 | analgesic (topical), antiseptic, antifungal | p10 10-1 | 3.09 | 5.56 | 4 | -0.36 | 0.04 | 4 | -28.5 |
| 428 | SAPPANONE A TRIMETHYL ETHER | 0 | C19H18O5 | 326.35 | 0 | p6 9-5 | 3.07 | 5.23 | 4 | 0.23 | 0.04 | 4 | 14.7 |
| 429 | HYMECHROME | 90-33-5 | C10H8O3 | 176.17 | choloretic, spasmolytic, sunscreen | p7 3-1 | 2.86 | 6.06 | 4 | -0.28 | 0.01 | 4 | -21.2 |
| 430 | CINNAMIC ACID | 621-82-9 | C9H8O2 | 148.16 | fragrance & flavoring agent | p4 3-1 | 2.86 | 6.06 | 4 | -0.39 | 0.01 | 4 | -31.0 |
| 431 | ACONITINE | 302-27-2 | C34H47NO11 | 645.75 | anesthetic (gastric), antipyretic, and cardiotoxin | p10 7-2 | 2.84 | 6.92 | 4 | -0.16 | 0.07 | 4 | -11.7 |
| 432 | GALANTAMINE | 357-70-0, 1953-04-4 [hydrobromide] | C17H21NO3 | 287.36 | anticholinesterase, analgesic, antiAlzheimer | p6 6-7 | 2.66 | 4.46 | 4 | -0.34 | 0.08 | 4 | -26.2 |
| 433 | PHENYLALANIINE (L) HYDROCHLORIDE | 63-91-2(base) | C9H12ClNO2 | 201.65 | amino acid | p9 10-7 | 2.59 | 10.09 | 4 | -0.12 | 0.08 | 4 | -8.5 |
| 434 | 4-O-METHYLPHLORACETOPHENONE | 7507-89-3 | C9H10O4 | 182.18 | antifungal | p4 9-7 | 2.57 | 9.05 | 4 | 0.16 | 0.12 | 4 | 10.4 |
| 435 | ERGONOVINE MALEATE | 129-51-1, 60-79-7 [ergonovine] | C23H27N3O6 | 441.49 | oxytocic, 5HT antagonist | p6 4-7 | 2.56 | 2.61 | 4 | 0.23 | 0.07 | 4 | 14.5 |
| 436 | ISOROTENONE | 0 | C23H22O6 | 394.43 | 0 | p1 2-7 | 2.53 | 6.12 | 4 | 0.71 | 0.16 | 4 | 38.9 |
| 437 | GLUTAMINE (D) | 6899-04-3 | C5H10N2O3 | 146.15 | 0 | p6 1-2 | 2.46 | 13.58 | 4 | -0.16 | 0.06 | 4 | -11.8 |
| 438 | PURPUROGALLIN-4-CARBOXYLIC ACID | 0 | C12H8O7 | 264.19 | antioxidant | p2 3-5 | 2.20 | 8.17 | 4 | 0.11 | 0.17 | 4 | 7.3 |
| 439 | URACIL | 66-22-8 | C4H4N2O2 | 112.09 | antineoplastic | p7 2-3 | 2.08 | 6.08 | 4 | -0.28 | 0.05 | 4 | -21.4 |
| 440 | PEUCENIN | 578-72-3 | C15H16O4 | 260.29 | 0 | p4 2-3 | 2.08 | 6.08 | 4 | -0.39 | 0.05 | 4 | -31.3 |
| 441 | NARINGIN | 10236-47-2 | C27H32O14 | 580.55 | antihaemorrhagic, antiinflammatory | p7 8-4 | 2.06 | 3.69 | 4 | 0.16 | 0.06 | 4 | 10.4 |
| 442 | ISOBERGAPTENE | 482-48-4 | C12H8O4 | 216.20 | 0 | p2 6-6 | 2.00 | 6.85 | 4 | 0.17 | 0.08 | 4 | 11.0 |
| 443 | CIANIDANOL | 154-23-4 | C15H14O6 | 290.28 | procollagen production inhibitoe, hepatoprotectant | p6 6-4 | 2.00 | 2.91 | 4 | -0.20 | 0.10 | 4 | -14.9 |
| 444 | BACCATIN III | 27548-93-2 | C31H38O11 | 586.64 | 0 | P2 8-5 | 1.76 | 6.79 | 4 | 0.08 | 0.03 | 4 | 5.2 |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 445 | MENTHYL BENZOATE | 0 | C17H24O2 | 260.38 | 0 | p7 3-4 | 1.74 | 4.94 | 4 | 0.24 | 0.06 | 4 | 15.1 |
| 446 | XANTHYLETIN | 553-19-5 | C14H12O3 | 228.25 | 0 | p4 3-4 | 1.74 | 4.94 | 4 | 0.12 | 0.06 | 4 | 8.1 |
| 447 | APOTOXICAROL | 0 | C18H14O7 | 342.31 | 0 | p7 9-4 | 1.64 | 2.64 | 4 | 0.16 | 0.07 | 4 | 10.7 |
| 448 | CAMPHOR (1R) | 464-49-3; 76-22-2 | C10H16O | 152.24 | analgesic, antiinfective, antipruritic | p7 4-3 | 1.63 | 3.26 | 4 | -0.22 | 0.04 | 4 | -16.2 |
| 449 | OBLIQUIN | 0 | C14H12O4 | 244.25 | 0 | p4 4-3 | 1.63 | 3.26 | 4 | -0.33 | 0.04 | 4 | -25.7 |
| 450 | RHODOCLADONIC ACID | 26984-15-6 | C15H10O8 | 318.24 | 0 | p1 8-2 | 1.58 | 7.53 | 4 | -0.03 | 0.09 | 4 | -2.1 |
| 451 | ROCCELLIC ACID | 22139-54-4 | C17H32O4 | 300.44 | 0 | p1 10-2 | 1.58 | 7.53 | 4 | -0.06 | 0.05 | 4 | -4.1 |
| 452 | HYGROMYCIN B | 31282-04-9 | C20H37N3O13 | 527.53 | antibacterial, anthelmintic; LD50 ip (rat) 63mg/Kg | p6 4-2 | 1.53 | 2.76 | 4 | 0.15 | 0.02 | 4 | 9.9 |
| 453 | GLYCYRRHIZIC ACID, AMMONIUM SALT | 1405-86-3 | C41H69N3O16 | 860.02 | 11beta-hydroxysteroid dehydrogenase inhibitor, antiinflammatory, expectorant, antihaemorrhagic, anti-HIV | p8 8-7 | 1.41 | 3.60 | 4 | -0.52 | 0.13 | 4 | -43.6 |
| 454 | 7,4'-DIMETHOXYISOFLAVONE | 0 | C17H14O4 | 282.30 | 0 | p8 5-3 | 1.31 | 16.35 | 4 | 0.04 | 0.08 | 4 | 3.0 |
| 455 | 6,3'-DIMETHOXYFLAVONE | 79786-40-6 | C17H14O4 | 282.30 | 0 | p9 8-6 | 1.27 | 13.51 | 4 | -0.08 | 0.11 | 4 | -5.6 |
| 456 | alpha-TOXICAROL (dl) | 82-09-7 | C23H22O7 | 410.43 | 0 | p7 2-4 | 0.92 | 7.28 | 4 | 0.01 | 0.16 | 4 | 0.6 |
| 457 | 2-METHYL GRAMINE | 0 | C12H16N2 | 188.27 | 0 | p4 2-4 | 0.92 | 7.28 | 4 | -0.11 | 0.16 | 4 | -7.5 |
| 458 | PIPERIC ACID | 5285-18-7 | C12H10O4 | 218.21 | 0 | p3 3-6 | 0.79 | 4.72 | 4 | -0.02 | 0.07 | 4 | -1.7 |
| 459 | INDOLE-3-CARBINOL | 700-06-1 | C9H9NO | 147.18 | antineoplastic; inhibitor of Amyloid-beta deposition | p5 1-5 | 0.77 | 4.37 | 4 | -0.40 | 0.12 | 4 | -31.7 |
| 460 | OXONITINE | 0 | C33H43NO12 | 645.71 | 0 | p4 8-3 | 0.75 | 4.78 | 4 | 0.05 | 0.05 | 4 | 3.3 |
| 461 | 12a-HYDROXY-9-DEMETHYLMUNDUSERONE -8-CARBOXYLIC ACID | 0 | C19H16O9 | 388.33 | 0 | p4 8-4 | 0.54 | 6.13 | 4 | 0.06 | 0.02 | 4 | 4.1 |
| 462 | SINAPIC ACID | 530-59-6 | C11H12O5 | 224.22 | 0 | p7 5-7 | 0.45 | 3.04 | 4 | 0.25 | 0.13 | 4 | 15.8 |
| 463 | XANTHONE | 90-47-1 | C13H8O2 | 196.21 | 0 | p4 5-7 | 0.45 | 3.04 | 4 | 0.13 | 0.13 | 4 | 8.9 |
| 464 | PERSEITOL HEPTAACETATE | 19147-10-5 | C21H30O14 | 506.46 | 0 | p9 5-5 | 0.17 | 3.78 | 4 | -0.14 | 0.04 | 4 | -10.1 |
| 465 | CHOLECALCIFEROL | 67-97-0 | C27H44O | 384.65 | vitamin D3 | p10 6-5 | 0.08 | 17.94 | 4 | -0.21 | 0.08 | 4 | -15.8 |
| 466 | AVOCADENE ACETATE | 24607-09-8 | C19H36O4 | 328.50 | antifungal, plant growth inhibitor | p9 1-4 | -0.39 | 8.75 | 4 | -0.47 | 0.14 | 4 | -38.4 |
| 467 | STICTIC ACID | 549-06-4 | C19H14O9 | 386.32 | 0 | P2 7-8 | -0.45 | 10.21 | 4 | 0.08 | 0.15 | 4 | 5.5 |
| 468 | BICUCULLINE(-) METHIODIDE | 55950-07-7 | C21H20INO6 | 509.30 | GABAa antagonist | p7 9-1 | -0.49 | 3.50 | 4 | -0.07 | 0.12 | 4 | -4.9 |
| 469 | EPICATECHIN | 490-46-0 | C15H14O6 | 290.28 | antioxidant | p9 10-1 | -0.62 | 3.01 | 4 | -0.09 | 0.04 | 4 | -6.3 |
| 470 | ALOIN | 5133-19-7 | C21H22O10 | 434.40 | cathartic, laxative | p6 6-1 | -0.73 | 14.69 | 4 | -0.63 | 0.12 | 4 | -54.3 |
| 471 | CLOVANEDIOL DIACETATE | 0 | C19H30O4 | 322.45 | 0 | P2 10-6 | -0.83 | 15.10 | 4 | 0.55 | 0.08 | 4 | 31.9 |
| 472 | CHAULMOOGRIC ACID, ETHYL ESTER | 623-32-5 | C20H36O2 | 308.51 | antilepretic | p6 7-6 | -0.95 | 4.76 | 4 | -0.15 | 0.02 | 4 | -10.8 |
| 473 | DIPTERYXIN | 53948-01-9 | C17H14O6 | 314.30 | 0 | p1 6-3 | -1.01 | 12.29 | 4 | -0.31 | 0.14 | 4 | -24.3 |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 474 | EPIGALLOCATECHIN 3,5-DIGALLATE | 0 | C29H22O15 | 610.49 | 0 | p9 8-3 | -1.19 | 4.93 | 4 | -0.23 | 0.04 | 4 | -17.5 |
| 475 | AJMALINE | 4360-17-7 | C20H26N2O2 | 326.44 | antiarrhythmic (Class Ia): inhibits glucose uptake by mitochondria, & PAF blocker | p3 10-6 | -1.24 | 6.91 | 4 | 0.10 | 0.08 | 4 | 6.9 |
| 476 | SALSOLINE | 89-31-6 | C11H15NO2 | 193.25 | antihypertensive, antihistamine | p9 8-5 | -1.38 | 13.01 | 4 | -0.01 | 0.09 | 4 | -0.9 |
| 477 | HYMECROMONE METHYL ETHER | 2555-28-4 | C11H10O3 | 190.20 | 0 | P2 9-2 | -1.44 | 21.29 | 4 | 0.26 | 0.05 | 4 | 16.6 |
| 478 | OSAJIN | 482-53-1 | C25H24O5 | 404.47 | 0 | p2 2-3 | -1.77 | 15.55 | 4 | -1.06 | 0.54 | 4 | -108.2 |
| 479 | PICROTIN | 21416-53-5 | C15H18O7 | 310.31 | GABAa receptor antagonist | p5 3-5 | -1.94 | 5.37 | 4 | -0.20 | 0.17 | 4 | -14.8 |
| 480 | EPIAFZELECHIN (2R,3R)(-) | 24808-04-6 | C15H14O5 | 274.28 | 0 | p3 3-7 | -2.10 | 11.70 | 4 | -0.14 | 0.18 | 4 | -10.2 |
| 481 | MANDELIC ACID, METHYL ESTER | 0 | C9H10O3 | 166.18 | 0 | p2 1-2 | -2.26 | 2.60 | 4 | 0.31 | 0.16 | 4 | 19.1 |
| 482 | CONESSINE | 5913-82-6, 546-06-5 [conessine] | C24H40N2 | 356.60 | antiamebic, antibacterial, antineoplastic, anesthetic (local) | p9 8-4 | -2.33 | 11.69 | 4 | -0.14 | 0.07 | 4 | -10.4 |
| 483 | HIERACIN | 1621-84-7 | C15H10O7 | 302.24 | 0 | p1 3-6 | -2.75 | 15.90 | 2 | 0.54 | 0.22 | 2 | 31.0 |
| 484 | EUPHOL | 514-47-6 | C30H50O | 426.73 | 0 | p9 8-7 | -2.84 | 9.90 | 4 | -0.29 | 0.04 | 4 | -22.5 |
| 485 | MENADIONE | 58-27-5 | C11H8O2 | 172.19 | prothrombogenic agent | p10 4-6 | -2.86 | 6.60 | 4 | 0.49 | 0.07 | 4 | 29.0 |
| 486 | AGMATINE SULFATE | 2482-00-0 | C5H16N4O4S | 228.27 | NMDA blocker, alpha-2 adrenergic agonist; NO synthase inhibitor | p5 10-7 | -2.93 | 14.78 | 4 | 0.21 | 0.17 | 4 | 13.5 |
| 487 | MUNDULONE ACETATE | 0 | C28H28O7 | 476.53 | 0 | p6 7-3 | -3.19 | 6.82 | 4 | 0.37 | 0.04 | 4 | 22.6 |
| 488 | CANAVANINE | 543-38-4 | C5H12N4O3 | 176.18 | NO synthase inhibitor | p5 5-6 | -3.40 | 5.55 | 4 | 0.29 | 0.05 | 4 | 18.4 |
| 489 | CARNITINE (dl) HYDROCHLORIDE | 461-06-3 | C7H16ClNO3 | 197.66 | antihyperlipoproteinemic, gastric/ pancreatic secretion stimulant | p8 6-1 | -3.41 | 16.17 | 4 | -0.79 | 0.04 | 4 | -73.4 |
| 490 | RIBOFLAVIN 5-PHOSPHATE SODIUM | 130-40-5 | C17H20N4NaO9P | 478.33 | vitamin, enzyme cofactor | p10 8-7 | -3.47 | 5.89 | 4 | -0.32 | 0.08 | 4 | -25.0 |
| 491 | MANGIFERIN | 4773-96-0 | C19H18O11 | 422.35 | MAO inhibitor, immunostimulant | p1 3-2 | -3.49 | 11.57 | 4 | 0.18 | 0.20 | 4 | 11.5 |
| 492 | N-METHYLISOLEUCINE | 5125-98-8 | C7H15NO2 | 145.20 | 0 | p9 9-1 | -3.51 | 17.39 | 4 | -0.07 | 0.05 | 4 | -5.2 |
| 493 | ACONITIC ACID | 585-84-2 | C6H6O6 | 174.11 | 0 | P2 7-7 | -3.59 | 5.97 | 4 | -0.01 | 0.10 | 4 | -0.7 |
| 494 | 4-METHYLESCULETIN | 0 | C10H8O4 | 192.17 | 0 | p8 2-7 | -3.64 | 20.21 | 4 | 0.01 | 0.13 | 4 | 0.7 |
| 495 | LANOSTEROL ACETATE | 0 | C32H52O2 | 468.77 | 0 | p3 1-2 | -3.78 | 4.86 | 4 | -0.04 | 0.16 | 4 | -2.8 |
| 496 | DIFFRACTAIC ACID | 436-32-8 | C20H22O7 | 374.39 | 0 | p1 5-6 | -3.80 | 8.68 | 4 | 0.91 | 0.21 | 4 | 46.7 |
| 497 | SITOSTERYL ACETATE | 0 | C31H52O2 | 456.76 | 0 | p4 7-2 | -3.86 | 7.26 | 4 | -0.17 | 0.12 | 4 | -12.4 |
| 498 | PANGAMIC ACID SODIUM | 20858-86-0 | C10H18NNaO8 | 303.25 | 0 | p8 8-4 | -4.04 | 4.03 | 4 | -0.69 | 0.11 | 4 | -61.0 |
| 499 | METHYL 7-DESHYDROXYPYROGALLIN -4-CARBOXYLATE | 77-41-8 | C13H10O6 | 262.22 | 0 | p3 9-3 | -4.08 | 8.73 | 4 | 0.16 | 0.16 | 4 | 10.5 |
| 500 | AMPHOTERICIN B | 1397-89-3 | C47H73NO17 | 924.10 | antifungal | p7 9-3 | -4.47 | 6.51 | 4 | 0.11 | 0.06 | 4 | 7.1 |
| 501 | VERBENALIN | 548-37-8 | C17H24O10 | 388.37 | cell growth inhibitor, coagulant | p8 9-3 | -4.48 | 7.07 | 4 | 2.45 | 1.77 | 4 | 81.7 |
| 502 | AGARIC ACID | 666-99-9 | C22H40O7 | 416.56 | antiperspirant | p3 9-5 | -4.50 | 6.51 | 4 | 0.30 | 0.07 | 4 | 18.9 |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 503 | CEDROL | 77-53-2 | C15H26O | 222.37 | acaricide | p7 6-4 | -4.53 | 8.49 | 4 | -0.11 | 0.07 | 4 | -7.7 |
| 504 | SENNOSIDE A | 81-27-6 | C42H38O20 | 862.76 | cathartic | p5 6-2 | -4.71 | 12.19 | 4 | -0.08 | 0.11 | 4 | -6.1 |
| 505 | PHYSOSTIGMINE SALICYLATE | 57-64-7, 57-47-6 [physostigmine] | C22H27N3O5 | 413.48 | cholinergic, anticholinesterase, miotic | p10 9-2 | -4.89 | 6.86 | 4 | -0.12 | 0.04 | 4 | -8.6 |
| 506 | PODOTOTARIN | 0 | C40H58O2 | 570.91 | 0 | p6 9-2 | -4.91 | 3.66 | 4 | 0.04 | 0.06 | 4 | 2.5 |
| 507 | CHAULMOOGRIC ACID | 502-30-7 | C18H32O2 | 280.45 | antibacterial (mycobacteria), antileprotic | p1 5-1 | -4.94 | 10.64 | 4 | -0.58 | 0.08 | 4 | -49.1 |
| 508 | GALANGIN 3-O-METHYL ETHER | 6665-74-3 | C16H12O5 | 284.27 | 0 | p5 2-8 | -5.04 | 2.62 | 4 | -0.54 | 0.10 | 4 | -45.3 |
| 509 | 2',4-DIHYDROXY-3,4',6'-TRIMETHOXYCHALCONE | 112572-59-5 | C18H18O6 | 330.34 | 0 | p7 4-6 | -5.12 | 7.47 | 4 | 0.09 | 0.03 | 4 | 5.9 |
| 510 | PISCIDIC ACID | 35388-57-9 | C11H12O7 | 256.21 | 0 | p4 4-6 | -5.12 | 7.47 | 4 | -0.03 | 0.03 | 4 | -1.7 |
| 511 | CORALYNE CHLORIDE | 38989-38-7 | C22H22ClNO4 | 399.88 | cytostatic, intercalating agent | p9 2-1 | -5.22 | 5.70 | 4 | -0.31 | 0.06 | 4 | -23.6 |
| 512 | ANETHOLE | 4180-23-8 | C10H12O | 148.21 | expectorant, gastric stimulant, insecticide | p10 10-6 | -5.30 | 5.83 | 4 | -0.08 | 0.06 | 4 | -5.8 |
| 513 | CAPSANTHIN | 465-42-9 | C40H56O3 | 584.89 | antineoplastic | p3 8-3 | -5.31 | 4.63 | 4 | -0.08 | 0.05 | 4 | -5.5 |
| 514 | EMBELIN | 0 | C17H26O4 | 294.39 | anthelmintic, oral contraceptive | p6 4-5 | -5.38 | 6.03 | 4 | 0.13 | 0.07 | 4 | 8.8 |
| 515 | GLUCOSAMINIC ACID | 3646-68-2 | C6H13NO6 | 195.17 | 0 | p7 4-5 | -5.48 | 1.58 | 4 | 0.22 | 0.03 | 4 | 13.9 |
| 516 | FUMARPROTOCETRARIC ACID | 489-50-9 | C22H16O12 | 472.37 | 0 | p4 4-5 | -5.48 | 1.58 | 4 | 0.10 | 0.03 | 4 | 6.9 |
| 517 | SPHONDIN | 483-66-9 | C12H8O4 | 216.20 | 0 | p7 9-5 | -5.49 | 8.01 | 4 | 0.32 | 0.09 | 4 | 20.1 |
| 518 | CELLOBIOSE (D[+]) | 528-50-7 | C12H22O11 | 342.30 | 0 | p1 4-5 | -5.56 | 11.11 | 4 | 0.91 | 0.15 | 4 | 46.9 |
| 519 | PHLORETIN | 60-82-2 | C15H14O5 | 274.28 | 0 | p1 9-1 | -5.73 | 13.60 | 4 | -0.15 | 0.06 | 4 | -10.8 |
| 520 | PSEUDO-ANISATIN | 31090-37-6 | C15H22O6 | 298.34 | GABA antagonist | p9 9-6 | -5.73 | 8.27 | 4 | 0.14 | 0.09 | 4 | 9.2 |
| 521 | 2,6-DIMETHOXYQUINONE | 35069-70-6 | C8H8O4 | 168.15 | antibacterial, induces dermatitis, mutagen | p9 7-3 | -5.86 | 5.05 | 4 | -0.06 | 0.05 | 4 | -4.3 |
| 522 | KHAYANTHONE | 25279-68-9 | C32H42O9 | 570.69 | 0 | p3 9-4 | -5.94 | 1.06 | 4 | -0.01 | 0.07 | 4 | -0.3 |
| 523 | SPECTINOMYCIN HYDROCHLORIDE | 22189-32-8, 21736-83-4 [anhydrous], 1695-77-8 [spectinomycin] | C14H26Cl2N2O7 | 405.28 | antibacterial | p10 6-3 | -6.16 | 18.84 | 4 | -0.51 | 0.13 | 4 | -42.8 |
| 524 | 3-PINANONE OXIME | 0 | C10H17NO | 167.25 | 0 | p6 7-4 | -6.18 | 3.64 | 4 | 0.02 | 0.11 | 4 | 1.5 |
| 525 | DESACETYLCOLFORSIN | 64657-20-1 | C20H32O6 | 368.47 | 0 | p9 9-4 | -6.53 | 4.67 | 4 | 0.22 | 0.03 | 4 | 14.3 |
| 526 | d-LIMONENE | 138-86-7 | C10H16 | 136.24 | skin irritant, sensitizer | p6 6-2 | -6.54 | 13.29 | 4 | -0.21 | 0.12 | 4 | -15.7 |
| 527 | 2',3-DIHYDROXY-4,4',6'-TRIMETHOXYCHALCONE | 38186-71-9 | C18H18O6 | 330.34 | 0 | p1 2-1 | -6.64 | 4.60 | 4 | -0.29 | 0.13 | 4 | -22.2 |
| 528 | NIACIN | 59-67-6 | C6H5NO2 | 123.11 | antihyperlipidemic, vitamin (enzyme cofactor) | p6 3-7 | -6.70 | 6.44 | 4 | 0.08 | 0.09 | 4 | 5.3 |
| 529 | ARECOLINE HYDROBROMIDE | 300-08-3, 63-75-2 [arecoline] | C8H14BrNO2 | 236.11 | anthelmintic (Cestodes), hypotensive, cathartic | p7 1-1 | -6.72 | 12.00 | 4 | -0.47 | 0.05 | 4 | -38.7 |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 530 | PRENYLETIN | 15870-91-4 | C14H14O4 | 246.27 | 0 | p4 1-1 | -6.72 | 12.00 | 4 | -0.59 | 0.05 | 4 | -50.0 |
| 531 | STRYCHNINE METHIODIDE | 0 | C22H25IN2O2 | 476.36 | neuromuscular blocker | P2 7-2 | -6.90 | 10.25 | 4 | 0.58 | 0.18 | 4 | 33.3 |
| 532 | CARYOPHYLLENE [t(-)] | 87-44-5 | C14H22 | 190.33 | 0 | p1 8-3 | -6.90 | 16.44 | 4 | 0.32 | 0.16 | 4 | 20.0 |
| 533 | ISOPOMIFERIN | 0 | C25H24O6 | 420.47 | 0 | p1 10-3 | -6.90 | 16.44 | 4 | -0.07 | 0.15 | 4 | -5.3 |
| 534 | alpha-HYDROXYDEOXYCHOLIC ACID | 83-49-8 | C24H40O4 | 392.58 | 0 | p1 5-2 | -6.93 | 15.75 | 4 | -0.52 | 0.10 | 4 | -43.0 |
| 535 | 1R,2S-PHENYLPROPYLAMINE | 14838-15-4 | C9H13NO | 151.21 | decongestant | p6 8-5 | -7.00 | 2.40 | 4 | -0.16 | 0.08 | 4 | -12.0 |
| 536 | ABSCISIC ACID (cis,trans; +/-) | 14375-45-2 | C15H20O4 | 264.32 | abscission-accelerant; kinetin neucleotide synthesis inhibitor | p1 6-5 | -7.09 | 30.70 | 4 | 0.65 | 0.45 | 3 | 36.3 |
| 537 | PALMIDROL | 544-31-0 | C18H37NO2 | 299.50 | antiinflammatory | p6 5-6 | -7.35 | 5.77 | 4 | 0.05 | 0.07 | 4 | 3.5 |
| 538 | ISOFORMONONETIN | 486-63-5 | C16H12O4 | 268.27 | 0 | p2 4-1 | -7.36 | 15.21 | 4 | -0.28 | 0.22 | 4 | -21.7 |
| 539 | EVOXINE | 522-11-2 | C18H21NO6 | 347.37 | 0 | p1 3-1 | -7.37 | 7.96 | 4 | 0.11 | 0.26 | 3 | 7.0 |
| 540 | SPERMINE | 71-44-3 | C10H26N4 | 202.35 | immune modulator | p1 5-3 | -7.42 | 7.35 | 4 | -0.43 | 0.20 | 4 | -35.1 |
| 541 | BILIRUBIN | 635-65-4 | C33H36N4O6 | 584.68 | 0 | p1 8-4 | -7.55 | 9.31 | 4 | -0.01 | 0.11 | 4 | -0.9 |
| 542 | MUUROLLADIE-3-ONE | 0 | C15H22O | 218.34 | 0 | p1 10-4 | -7.55 | 9.31 | 4 | -0.02 | 0.07 | 4 | -1.7 |
| 543 | MANGOSTIN TRIMETHYL ETHER | 0 | C27H32O6 | 452.55 | 0 | p3 5-6 | -8.08 | 6.81 | 4 | 0.00 | 0.03 | 4 | -0.1 |
| 544 | DIHYDROJASMONIC ACID, METHYL ESTER | 24851-98-7 | C13H22O3 | 226.32 | plant growth regulator | p8 3-2 | -8.77 | 11.62 | 4 | -0.06 | 0.07 | 4 | -4.0 |
| 545 | ENOXOLONE | 471-53-4 | C30H46O4 | 470.70 | antitussive, antiinflammatory, antibacterial | p6 3-6 | -8.81 | 2.02 | 4 | -0.07 | 0.05 | 4 | -5.3 |
| 546 | CHRYSAROBIN | 491-58-7 | C15H12O3 | 240.26 | 0 | p7 10-6 | -8.96 | 6.12 | 4 | 0.48 | 0.07 | 4 | 28.2 |
| 547 | GENKWANIN | 437-64-9 | C16H12O5 | 284.27 | 0 | p8 6-2 | -9.13 | 28.74 | 4 | -0.83 | 0.06 | 4 | -77.7 |
| 548 | ADENINE | 73-24-5 | C5H5N5 | 135.13 | Vitamin B4 | p10 2-5 | -9.27 | 4.53 | 4 | -0.08 | 0.12 | 4 | -5.9 |
| 549 | EPITHEAFLAVIC ACID | 0 | C21H16O10 | 428.36 | 0 | p1 1-8 | -9.36 | 20.34 | 4 | 0.10 | 0.04 | 4 | 6.9 |
| 550 | TOTAROL | 511-15-9 | C20H30O | 286.46 | 0 | p2 4-6 | -9.45 | 5.71 | 4 | -0.36 | 0.10 | 4 | -28.4 |
| 551 | 3,4',5,6,7-PENTAMETHOXYFLAVONE | 4472-73-5 | C20H20O7 | 372.38 | 0 | p3 8-6 | -9.57 | 2.71 | 4 | 0.24 | 0.04 | 4 | 15.6 |
| 552 | NIACINAMIDE | 98-92-0 | C6H6N2O | 122.13 | Vitamin B3; enzyme cofactor; anti-pellagra | p6 10-7 | -9.59 | 6.64 | 4 | -0.05 | 0.05 | 4 | -3.6 |
| 553 | LEVODOPA | 59-92-7 | C9H11NO4 | 197.19 | antiparkinsonian | p7 6-1 | -9.67 | 12.17 | 4 | -0.21 | 0.16 | 4 | -15.4 |
| 554 | PAEONOL | 552-41-0 | C9H10O3 | 166.18 | antibacterial | p2 3-7 | -10.37 | 19.61 | 4 | 0.01 | 0.12 | 4 | 0.8 |
| 555 | CYCLOSERINE (D) | 68-41-7 | C3H6N2O2 | 102.09 | antibacterial (tuberculostatic) | p10 1-1 | -10.45 | 9.82 | 4 | -0.38 | 0.13 | 4 | -30.0 |
| 556 | CINCHONINE | 118-10-5 | C19H22N2O | 294.40 | antimalarial | p8 5-4 | -10.47 | 18.05 | 4 | 0.01 | 0.12 | 4 | 0.4 |
| 557 | VERATRIC ACID | 93-07-2 | C9H10O4 | 182.18 | 0 | p9 4-4 | -10.65 | 2.87 | 4 | -0.09 | 0.02 | 4 | -6.7 |
| 558 | ERGOSTEROL ACETATE | 2418-45-3 | C32H50O2 | 466.75 | 0 | p5 8-1 | -10.68 | 11.05 | 4 | 0.06 | 0.12 | 4 | 3.7 |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 559 | DIFUCOL HEXAMETHYL ETHER | 14262-07-8 | C18H22O6 | 334.37 | 0 | p3 4-7 | -10.90 | 5.62 | 4 | 0.08 | 0.09 | 4 | 5.1 |
| 560 | CORTISONE | 53-06-5 | C21H28O5 | 360.45 | antiinflammatory, glucocorticoid | p6 2-6 | -10.93 | 6.03 | 4 | -0.17 | 0.07 | 4 | -12.8 |
| 561 | DEOXYSAPPANONE B 7,3'-DIMETHYL ETHER | 0 | C18H18O5 | 314.34 | 0 | p5 9-2 | -11.00 | 6.96 | 4 | 0.03 | 0.04 | 4 | 2.2 |
| 562 | 8-HYDROXYCARAPINIC ACID | 0 | C26H30O8 | 470.52 | 0 | p1 6-7 | -11.03 | 10.14 | 4 | 1.43 | 0.22 | 4 | 63.0 |
| 563 | 2',2'-BISEPIGALLOCATECHIN DIGALLATE | 0 | C44H34O22 | 914.75 | 0 | p6 1-1 | -11.23 | 5.23 | 4 | -0.51 | 0.10 | 4 | -42.3 |
| 564 | 7-AMINOCEPHALOSPORANIC ACID | 957-68-6 | C10H12N2O5S | 272.28 | 0 | p1 3-3 | -11.44 | 6.56 | 4 | 0.19 | 0.26 | 4 | 12.1 |
| 565 | KHELLIN | 82-02-0 | C14H12O5 | 260.25 | vasodilator (coronary), photosensitizer | p6 4-6 | -11.76 | 6.37 | 4 | 0.22 | 0.07 | 4 | 14.1 |
| 566 | POLYMYXIN B SULFATE | 1405-20-5, 1404-26-8 [polymyxin B] | C56H100N16O17S | 1301.58 | antibacterial | p10 1-3 | -11.86 | 13.49 | 4 | -0.20 | 0.12 | 4 | -15.1 |
| 567 | DIHYDROFOLIC ACID | 4033-27-6 | C19H21N7O6 | 443.42 | antidote to methotrexate toxicity | p7 1-3 | -11.92 | 5.99 | 4 | -0.36 | 0.07 | 4 | -28.7 |
| 568 | XYLOCARPUS A | 0 | C31H38O11 | 586.64 | 0 | p4 1-3 | -11.92 | 5.99 | 4 | -0.48 | 0.07 | 4 | -39.2 |
| 569 | PIPERINE | 94-62-2 | C17H19NO3 | 285.35 | analeptic, antibacterial | p10 8-5 | -12.09 | 6.44 | 4 | 0.03 | 0.07 | 4 | 2.1 |
| 570 | BRAZILEIN | 600-76-0 | C16H12O5 | 284.27 | 0 | p6 8-3 | -12.20 | 6.49 | 4 | 0.03 | 0.04 | 4 | 2.2 |
| 571 | SPIRAMYCIN | 8025-81-8 | C43H74N2O14 | 843.07 | antibacterial | p10 10-5 | -12.26 | 13.32 | 4 | -0.17 | 0.07 | 4 | -12.2 |
| 572 | MEROGEDUNIN | 0 | C21H28O4 | 344.45 | 0 | p1 7-4 | -12.28 | 11.90 | 4 | -0.50 | 0.05 | 3 | -41.1 |
| 573 | ICARIIN | 489-32-7 | C33H40O15 | 676.68 | hepatoprotective | p4 10-1 | -12.33 | 2.62 | 4 | -0.22 | 0.06 | 4 | -16.4 |
| 574 | LEVOTHYROXINE | 51-48-9 | C15H11I4NO4 | 776.88 | antihypercholesterimic, thyromimetic | p10 8-2 | -12.41 | 11.60 | 4 | -0.03 | 0.01 | 4 | -2.2 |
| 575 | TOTAROL-19-CARBOXYLIC ACID, METHYL ESTER | 0 | C21H30O3 | 330.47 | 0 | p8 4-6 | -12.62 | 27.41 | 4 | 0.37 | 0.12 | 4 | 22.4 |
| 576 | PURPUROGALLIN | 569-77-7 | C11H8O5 | 220.18 | xanthine oxidase inhibitor, antioxidant | p3 3-2 | -12.64 | 8.05 | 4 | -0.01 | 0.10 | 4 | -0.7 |
| 577 | 18alpha-GLYCYRRHETINIC ACID | 0 | C30H46O4 | 470.70 | antiinflammatory | p5 4-6 | -12.69 | 1.33 | 4 | -0.01 | 0.05 | 4 | -0.5 |
| 578 | ISOPEONOL | 493-33-4 | C9H10O3 | 166.18 | 0 | p7 3-7 | -12.83 | 6.96 | 4 | 0.03 | 0.07 | 4 | 2.3 |
| 579 | N-METHYLBENZYLAMINE HYDROCHLORIDE | 13426-94-3, 103-67-3(base) | C8H12ClN | 157.64 | 0 | p4 3-7 | -12.83 | 6.96 | 4 | -0.08 | 0.07 | 4 | -5.7 |
| 580 | PHYTOL | 0 | C19H38O | 282.51 | 0 | p3 6-2 | -12.94 | 12.06 | 4 | -0.42 | 0.12 | 4 | -33.6 |
| 581 | BAICALIN | 21967-41-9 | C21H18O11 | 446.37 | diuretic | p1 8-8 | -13.01 | 3.92 | 4 | -0.23 | 0.21 | 4 | -17.1 |
| 582 | SMILAGENIN ACETATE | 0 | C29H46O4 | 458.69 | 0 | p1 1-4 | -13.03 | 6.86 | 4 | -0.11 | 0.13 | 4 | -7.9 |
| 583 | IRIDIN | 491-74-7 | C24H26O13 | 522.47 | 0 | p5 3-2 | -13.32 | 6.11 | 4 | -0.14 | 0.08 | 4 | -10.0 |
| 584 | ADENOSINE | 58-61-7 | C10H13N5O4 | 267.25 | antiarrhythmic, cardiac depressant | p3 10-5 | -13.39 | 5.77 | 4 | 0.02 | 0.09 | 4 | 1.5 |
| 585 | IRIGENOL | 4935-93-7 | C15H10O8 | 318.24 | 0 | p5 7-3 | -13.42 | 14.28 | 4 | 0.01 | 0.13 | 4 | 0.7 |
| 586 | CHRYSANTHEMIC ACID | 10453-89-1 | C10H16O2 | 168.24 | esters as insecticide | p8 7-5 | -13.45 | 15.60 | 4 | -0.32 | 0.12 | 4 | -24.6 |
| 587 | DUARTIN, DIMETHYL ETHER | 0 | C20H24O6 | 360.41 | 0 | p5 5-4 | -13.50 | 4.27 | 4 | -0.22 | 0.07 | 4 | -16.4 |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 588 | alpha-TOCHOPHERYL ACETATE | 58-95-7 | C31H52O3 | 472.76 | vitamin E | p7 6-2 | -13.55 | 13.85 | 4 | -0.21 | 0.17 | 4 | -15.8 |
| 589 | NOVOBIOCIN SODIUM | 1476-53-5, 303-81-1 [novobiocin] | C31H35N2NaO11 | 634.62 | antibacterial | p1 3-8 | -13.64 | 14.42 | 4 | 0.10 | 0.12 | 4 | 6.5 |
| 590 | MENAQUINONE-4 | 0 | C21H24O2 | 308.42 | antioxidant, alkaline phosphatase enhancer | p7 8-5 | -13.76 | 12.84 | 4 | 0.06 | 0.13 | 4 | 4.1 |
| 591 | 5alpha-ANDROSTAN-3,17-DIONE | 0 | C19H28O2 | 288.43 | androgen | p5 5-8 | -13.88 | 11.20 | 4 | 0.00 | 0.04 | 4 | -0.1 |
| 592 | CHOLESTERYL BENZOATE | 604-32-0 | C34H50O2 | 490.78 | 0 | p6 4-4 | -14.05 | 6.04 | 4 | 0.08 | 0.06 | 4 | 5.3 |
| 593 | CHLORTETRACYCLINE HYDROCHLORIDE | 64-72-2 | C22H24Cl2N2O8 | 515.35 | antibacterial, antiamebic, Ca chelator, hepatotoxic; inhibits protein synthesis | p7 10-3 | -14.12 | 2.48 | 4 | -0.03 | 0.05 | 4 | -2.0 |
| 594 | 4-ACETOXYPHENOL | 3233-32-7 | C8H8O3 | 152.15 | antioxidant | p3 7-1 | -14.14 | 5.77 | 4 | 0.21 | 0.04 | 4 | 13.4 |
| 595 | MUCIC ACID | 526-99-8 | C6H10O8 | 210.14 | 0 | p8 4-3 | -14.31 | 11.79 | 4 | -0.19 | 0.08 | 4 | -13.8 |
| 596 | KYNURENINE | 0 | C10H12N2O3 | 208.22 | 0 | P2 10-5 | -14.37 | 9.37 | 4 | 0.48 | 0.24 | 4 | 28.1 |
| 597 | COTARNINE CHLORIDE | 10018-19-6, 82-54-2 [cotarnine] | C12H14ClNO3 | 255.70 | vasoconstrictor | p4 10-3 | -14.54 | 8.04 | 4 | -0.20 | 0.08 | 4 | -15.2 |
| 598 | PRIMULETIN | 491-78-1 | C15H10O3 | 238.25 | 0 | p4 8-2 | -14.55 | 11.94 | 4 | 0.05 | 0.04 | 4 | 3.1 |
| 599 | SPARTEINE SULFATE | 6160-12-9, 299-39-8 [anhydrous] | C15H28N2O4S | 332.47 | oxytocic | p7 7-1 | -14.55 | 7.38 | 4 | 0.04 | 0.16 | 4 | 3.0 |
| 600 | ELLAGIC ACID | 476-66-4 | C14H6O8 | 302.20 | hemostatic, antineoplastic, antimutagenic | p7 8-1 | -14.62 | 5.34 | 4 | -0.05 | 0.06 | 4 | -3.6 |
| 601 | SOLIDAGENONE | 23534-56-7 | C20H28O3 | 316.44 | 0 | p2 1-7 | -14.64 | 11.96 | 4 | 0.73 | 0.26 | 4 | 39.6 |
| 602 | alpha-TOCHOPHEROL | 59-02-9 | C29H50O2 | 430.72 | vitamin E, antioxidant | P2 10-4 | -14.67 | 19.84 | 4 | 0.21 | 0.27 | 4 | 13.8 |
| 603 | N-METHYLANTHRANILIC ACID | 119-68-6 | C8H9NO2 | 151.17 | 0 | P2 8-4 | -14.80 | 16.62 | 4 | 0.20 | 0.04 | 4 | 13.0 |
| 604 | GALANGIN | 548-83-4 | C15H10O5 | 270.24 | CYP1A1 inhibitor | P2 10-1 | -14.90 | 21.99 | 4 | 0.39 | 0.07 | 4 | 23.6 |
| 605 | IRETOL | 0 | C7H8O4 | 156.14 | 0 | p6 1-4 | -15.02 | 9.00 | 4 | -0.32 | 0.07 | 4 | -24.7 |
| 606 | IRIGENIN | 548-76-5 | C18H16O8 | 360.32 | 0 | p5 2-2 | -15.03 | 12.03 | 4 | -0.43 | 0.14 | 4 | -34.9 |
| 607 | QUININE SULFATE | 6119-70-6, 804-63-7 [anhydrous], 130-95-0 [quinine] | C20H26N2O6S | 422.50 | antimalarial, skeletal muscle relaxant | p10 3-3 | -15.40 | 5.39 | 4 | -0.12 | 0.06 | 4 | -8.7 |
| 608 | RHODINYL ACETATE | 0 | C12H22O2 | 198.31 | 0 | P2 9-7 | -15.58 | 8.00 | 4 | 0.17 | 0.15 | 4 | 10.9 |
| 609 | AMYGDALIN | 29883-15-6 | C20H27NO11 | 457.44 | antiinflammatory, experimental antineoplastic | p8 6-7 | -15.61 | 20.76 | 4 | 0.07 | 0.04 | 4 | 4.8 |
| 610 | UMBELLIFERONE | 93-35-6 | C9H6O3 | 162.15 | antifungal, phytoalexin | p2 2-5 | -15.67 | 2.30 | 4 | -0.92 | 0.57 | 4 | -88.9 |
| 611 | IRIGENIN, DIBENZYL ETHER | 0 | C32H28O8 | 540.58 | 0 | p9 8-2 | -15.69 | 8.14 | 4 | 0.00 | 0.07 | 4 | 0.0 |
| 612 | 15-NORCARYOPHYLLEN-3-ONE | 0 | C14H22O | 206.33 | 0 | p6 8-4 | -15.72 | 5.09 | 4 | -0.05 | 0.11 | 4 | -3.6 |
| 613 | S-ISOCORYDINE (+) | 475-67-2 | C20H23NO4 | 341.41 | sedative, cholinergic | p1 9-4 | -15.72 | 13.54 | 4 | -0.56 | 0.99 | 4 | -47.4 |
| 614 | DICTAMNINE | 484-29-7 | C12H9NO2 | 199.21 | 0 | p3 3-4 | -15.89 | 10.75 | 4 | 0.06 | 0.03 | 4 | 3.8 |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 615 | METHYL 7-DESOXYPURPUROGALLIN-7-CARBOXYLATE TRIMETHYL ETHER | 0 | C16H16O6 | 304.30 | 0 | p9 3-3 | -15.95 | 3.03 | 4 | 0.00 | 0.08 | 4 | 0.1 |
| 616 | PERILLIC ACID (-) | 7694-45-3 | C10H14O2 | 166.22 | inhibits posttranslational cys isoprenylation, blocks G-protein | p5 10-6 | -16.19 | 10.71 | 4 | 0.14 | 0.16 | 4 | 8.9 |
| 617 | MELIBIOSE | 585-99-9 | C12H22O11 | 342.30 | 0 | p6 7-2 | -16.19 | 7.01 | 4 | -0.06 | 0.07 | 4 | -4.0 |
| 618 | N-ACETYLMURAMIC ACID | 10597-89-4 | C11H19NO8 | 293.28 | 0 | p6 2-3 | -16.52 | 6.87 | 4 | -0.11 | 0.08 | 4 | -8.2 |
| 619 | DIGITONIN | 11024-24-1 | C56H92O29 | 1229.34 | 0 | p8 4-2 | -16.58 | 11.21 | 4 | -0.12 | 0.03 | 4 | -8.8 |
| 620 | MELEZITOSE | 0 | C18H32O16 | 504.45 | 0 | p9 3-1 | -16.81 | 5.47 | 4 | -0.18 | 0.06 | 4 | -13.0 |
| 621 | CHRYSANTHEMYL ALCOHOL | 5617-92-5 | C10H18O | 154.25 | 0 | p9 4-1 | -16.89 | 6.13 | 4 | -0.13 | 0.02 | 4 | -9.5 |
| 622 | 7,2'-DIHYDROXYFLAVONE | 77298-66-9 | C15H10O4 | 254.24 | antihaemorrhagic | p8 5-8 | -16.96 | 7.55 | 4 | 0.19 | 0.09 | 4 | 12.6 |
| 623 | gamma-AMINOBUTYRIC ACID | 56-12-2 | C4H9NO2 | 103.12 | antihypertensive | p6 5-5 | -17.05 | 6.18 | 4 | 0.04 | 0.03 | 4 | 2.6 |
| 624 | NONIC ACID | 0 | C9H16O4 | 188.23 | 0 | p5 8-3 | -17.10 | 4.83 | 4 | 0.06 | 0.03 | 4 | 3.9 |
| 625 | 7-METHOXYCHROMONE | 0 | C10H8O3 | 176.17 | 0 | p3 10-1 | -17.15 | 5.76 | 4 | -0.34 | 0.04 | 4 | -26.1 |
| 626 | TETRACYCLINE HYDROCHLORIDE | 64-75-5, 60-54-8 [tetracycline] | C22H25ClN2O8 | 480.91 | antibacterial, antiamebic, antirickettsial | p10 8-3 | -17.26 | 6.52 | 4 | -0.31 | 0.02 | 4 | -24.3 |
| 627 | LACTOBIONIC ACID | 96-82-2 | C12H22O12 | 358.30 | food additive | p3 7-2 | -17.48 | 3.56 | 4 | -0.35 | 0.09 | 4 | -27.5 |
| 628 | GOSSYPETIN | 489-35-0 | C15H10O8 | 318.24 | 0 | p5 5-2 | -17.52 | 7.12 | 4 | -0.04 | 0.08 | 4 | -2.6 |
| 629 | MYOSMINE | 532-12-7 | C9H10N2 | 146.19 | mitogen | p6 5-3 | -17.55 | 3.79 | 4 | 0.07 | 0.03 | 4 | 4.5 |
| 630 | JUGLONE | 481-39-0 | C10H6O3 | 174.16 | antineoplastic, antifungal | p7 8-6 | -17.67 | 5.66 | 4 | 0.17 | 0.04 | 4 | 11.2 |
| 631 | STIGMASTEROL | 0 | C29H48O | 412.71 | 0 | p1 4-6 | -17.97 | 27.51 | 4 | 0.96 | 0.10 | 4 | 48.6 |
| 632 | EMODIN | 518-82-1 | C15H10O5 | 270.24 | antibacterial, antineoplastic, cathartic, tyrosine kinase inhibitor | p3 6-3 | -17.99 | 7.24 | 4 | -0.04 | 0.07 | 4 | -3.0 |
| 633 | 1-HYDROXY-3,6,7-TRIMETHOXY-2,8-DIPRENYLXANTHONE | 15404-76-9 | C26H30O6 | 438.53 | 0 | p3 4-6 | -18.05 | 4.77 | 4 | 0.12 | 0.15 | 4 | 7.7 |
| 634 | THEOBROMINE | 83-67-0 | C7H8N4O2 | 180.17 | diuretic, bronchodilator, cardiotonic | P2 8-3 | -18.14 | 6.74 | 4 | 0.03 | 0.09 | 4 | 2.2 |
| 635 | GALANGIN TRIMETHYL ETHER | 26964-29-4 | C18H16O5 | 312.33 | 0 | p3 9-2 | -18.22 | 2.52 | 4 | 0.13 | 0.11 | 4 | 8.8 |
| 636 | ISOTECTORIGENIN, 7-METHYL ETHER | 0 | C18H16O6 | 328.32 | 0 | p4 10-5 | -18.66 | 5.87 | 4 | 0.04 | 0.05 | 4 | 3.0 |
| 637 | ASTRAGALOSIDE IV | 84687-43-4 | C41H68O14 | 784.99 | 0 | p1 5-8 | -18.98 | 33.36 | 4 | -0.19 | 0.07 | 4 | -14.1 |
| 638 | 2',4'-DIHYDROXYCHALCONE 4'-GLUCOSIDE | 0 | C21H22O8 | 402.40 | anthelmintic & antiulcerocenic | p1 4-8 | -19.50 | 24.66 | 4 | 0.03 | 0.19 | 4 | 1.9 |
| 639 | AVOCADYNOFURAN | 24708-33-6 | C17H26O | 246.40 | 0 | p5 7-2 | -19.78 | 21.92 | 4 | 0.02 | 0.10 | 4 | 1.4 |
| 640 | PEONIFLORIN | 23180-57-6 | C23H30O11 | 482.49 | antiinflammatory, antispasmodic, antihypertensive, antidiuretic | p8 3-4 | -19.87 | 6.80 | 4 | -0.11 | 0.10 | 4 | -7.6 |
| 641 | KAINIC ACID | 487-79-6 | C10H15NO4 | 213.24 | glutamate receptor agonist, anthelmintic | p7 7-2 | -19.89 | 9.21 | 4 | -0.04 | 0.08 | 4 | -2.6 |
| 642 | HELENINE | 546-43-0 | C15H20O2 | 232.33 | anthelmintic, antibacterial, antineoplastic | p7 5-5 | -19.97 | 8.59 | 4 | 0.10 | 0.10 | 4 | 6.4 |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 643 | LECANORIC ACID | 480-56-8 | C16H14O7 | 318.29 | 0 | p4 5-5 | -19.97 | 8.59 | 4 | -0.02 | 0.10 | 4 | -1.2 |
| 644 | 3beta-HYDROXY-23,24-BISNORCHOL-5-ENIC ACID | 0 | C22H34O3 | 346.51 | 0 | p3 5-1 | -20.26 | 8.34 | 4 | -0.71 | 0.01 | 4 | -63.2 |
| 645 | MADECASSIC ACID | 18449-41-7 | C30H48O6 | 504.71 | wound healing | p1 9-8 | -20.30 | 17.06 | 4 | -0.16 | 0.13 | 4 | -11.7 |
| 646 | THREONINE (L) | 72-19-5 | C4H9NO3 | 119.12 | amino acid, nutrient | p7 10-1 | -20.50 | 11.38 | 4 | -0.26 | 0.10 | 4 | -19.5 |
| 647 | HISTAMINE DIHYDROCHLORIDE | 51-45-6 [histamine] | C5H11Cl2N3 | 184.07 | H1&2 agonist, edema induction, gastric secretion stimulant | p10 3-2 | -20.59 | 14.84 | 4 | 0.02 | 0.08 | 4 | 1.3 |
| 648 | NEROL | 106-25-2 | C10H18O | 154.25 | weak estrogen receptor blocker | p5 9-6 | -20.59 | 7.59 | 4 | 0.43 | 0.09 | 4 | 25.8 |
| 649 | PROTOPORPHYRIN IX | 553-12-8 | C34H34N4O4 | 562.67 | hepatoprotectant | p8 2-6 | -20.60 | 28.20 | 4 | 0.00 | 0.20 | 4 | -0.1 |
| 650 | PTAEROXYLIN | 14729-11-4 | C15H14O4 | 258.28 | 0 | p4 7-3 | -20.69 | 5.56 | 4 | -0.13 | 0.08 | 4 | -9.7 |
| 651 | XANTHOXYLIN | 90-24-4 | C10H12O4 | 196.20 | 0 | p3 4-5 | -20.73 | 2.33 | 4 | 0.08 | 0.04 | 4 | 5.4 |
| 652 | VINCAMINE | 1617-90-9 | C21H26N2O3 | 354.45 | vasodilator | p6 5-4 | -20.79 | 8.57 | 4 | 0.12 | 0.06 | 4 | 8.2 |
| 653 | NORSTICTIC ACID | 571-67-5 | C18H12O9 | 372.29 | antibacterial | p6 2-1 | -20.79 | 12.81 | 4 | -0.18 | 0.09 | 4 | -13.4 |
| 654 | SINAPIC ACID METHYL ETHER | 90-50-6 | C12H14O5 | 238.24 | 0 | p1 5-5 | -20.82 | 14.35 | 4 | 0.66 | 0.12 | 3 | 36.6 |
| 655 | PECTOLINARIN | 28978-02-1 | C29H34O15 | 622.59 | 0 | p4 9-5 | -20.96 | 9.20 | 4 | 1.99 | 1.75 | 4 | 74.8 |
| 656 | YOHIMBIC ACID HYDRATE | 522-87-2 | C20H26N2O4 | 358.44 | 0 | p6 2-5 | -21.23 | 3.47 | 4 | -0.27 | 0.06 | 4 | -20.7 |
| 657 | 2',4-DIHYDROXYCHALCONE | 13323-66-5 | C15H12O3 | 240.26 | 0 | p5 10-3 | -21.40 | 13.06 | 4 | 0.13 | 0.13 | 4 | 8.3 |
| 658 | AVOCADENOFURAN | 25346-24-1 | C17H28O | 248.41 | 0 | p6 6-3 | -21.47 | 25.05 | 4 | -0.41 | 0.09 | 4 | -32.5 |
| 659 | GOSSYPOL-ACETIC ACID COMPLEX | 0 | C32H34O10 | 578.62 | male contraceptive | p6 10-1 | -21.55 | 10.62 | 4 | -0.10 | 0.06 | 4 | -7.1 |
| 660 | GANGALEOIDIN | 55365-63-4 | C18H14Cl2O7 | 413.21 | 0 | p8 4-5 | -21.59 | 19.44 | 4 | -0.05 | 0.18 | 4 | -3.3 |
| 661 | DEHYDRODIHYDROROTENONE | 6659-45-6 | C23H22O6 | 394.43 | 0 | P2 8-7 | -21.64 | 13.80 | 4 | 0.06 | 0.12 | 4 | 4.4 |
| 662 | BACITRACIN | 1405-87-4 | C66H103N17O16S | 1422.73 | antibacterial | p7 8-2 | -21.81 | 8.19 | 4 | 0.02 | 0.06 | 4 | 1.4 |
| 663 | OSAJIN 4'-METHYL ETHER | 27762-88-5 | C26H26O5 | 418.49 | 0 | p8 5-7 | -21.87 | 15.35 | 4 | -0.04 | 0.06 | 4 | -2.7 |
| 664 | MIMOSINE | 0 | C8H10N2O4 | 198.18 | depilatory agent | p8 4-8 | -22.01 | 14.13 | 4 | -0.01 | 0.11 | 4 | -0.4 |
| 665 | GOSSYPIN | 652-78-8 | C21H20O13 | 480.39 | 0 | p5 5-5 | -22.05 | 9.68 | 4 | -0.07 | 0.08 | 4 | -4.8 |
| 666 | BERGAPTEN | 484-20-8 | C12H8O4 | 216.20 | antipsoriatic, antiinflammatory | p6 3-5 | -22.30 | 11.50 | 4 | 0.06 | 0.05 | 4 | 4.3 |
| 667 | LANOSTEROL | 79-63-0 | C30H50O | 426.73 | 0 | p9 6-4 | -22.47 | 9.27 | 4 | -0.24 | 0.23 | 4 | -18.1 |
| 668 | CEAROIN | 52811-37-7 | C14H12O4 | 244.25 | 0 | p8 8-3 | -22.53 | 5.49 | 4 | -0.27 | 0.20 | 4 | -21.0 |
| 669 | LYSINE (L) HYDROCHLORIDE | 657-27-2 | C6H15ClN2O2 | 182.65 | amino acid, nutrient | p9 5-4 | -22.55 | 8.13 | 4 | -0.15 | 0.04 | 4 | -11.0 |
| 670 | TANNIC ACID | 1401-55-4 | C76H52O46 | 1701.23 | nonspecific enzyme/receptor blocker | p6 5-8 | -22.61 | 8.28 | 4 | 0.27 | 0.05 | 4 | 17.0 |
| 671 | GUAIOL(-) | 489-86-1 | C15H26O | 222.37 | 0 | p6 8-2 | -22.71 | 13.37 | 4 | 0.20 | 0.09 | 4 | 12.7 |
| 672 | PROLINE (L) | 147-85-3 | C5H9NO2 | 115.13 | amino acid, nutrient | p9 9-2 | -22.72 | 4.93 | 4 | 0.03 | 0.06 | 4 | 1.9 |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 673 | CHOLESTERYL ACETATE | 604-35-3 | C29H48O2 | 428.70 | 0 | p8 2-3 | -22.86 | 10.92 | 4 | -0.08 | 0.09 | 4 | -5.8 |
| 674 | 3,4'-DIMETHOXYFLAVONE | 0 | C17H14O4 | 282.30 | 0 | p4 10-7 | -22.87 | 7.48 | 4 | 0.36 | 0.06 | 4 | 22.3 |
| 675 | PUERARIN | 3681-99-0 | C21H20O9 | 416.39 | beta-adrenergic blocker | p2 2-6 | -22.97 | 9.51 | 4 | -0.46 | 0.56 | 4 | -37.4 |
| 676 | ISOPIMPINELLIN | 482-27-9 | C13H10O5 | 246.22 | 0 | p3 2-2 | -23.17 | 11.47 | 4 | -0.24 | 0.01 | 4 | -18.1 |
| 677 | HARMANE | 486-84-0 | C12H10N2 | 182.23 | intercalating agent, sedative | p6 9-3 | -23.18 | 8.01 | 4 | 0.07 | 0.03 | 4 | 4.5 |
| 678 | 5alpha-CHOLESTANOL | 80-97-7 | C27H48O | 388.68 | 0 | p3 5-4 | -23.23 | 4.52 | 4 | -0.03 | 0.05 | 4 | -2.4 |
| 679 | LINALOOL (+) | 0 | C10H18O | 154.25 | 0 | p6 10-4 | -23.26 | 4.26 | 4 | 0.09 | 0.10 | 4 | 6.1 |
| 680 | HYDRASTINE (1R, 9S) | 118-08-1 | C21H21NO6 | 383.40 | antihypertensive, sedative, antibacterial | p10 10-4 | -23.62 | 10.12 | 4 | -0.18 | 0.04 | 4 | -13.2 |
| 681 | VIOLASTYRENE | 19034-96-9 | C17H18O3 | 270.33 | 0 | p5 3-3 | -23.64 | 6.82 | 4 | -0.30 | 0.14 | 4 | -23.3 |
| 682 | 4-METHYLDAPHNETIN | 2107-77-9 | C10H8O4 | 192.17 | 0 | p8 1-7 | -23.67 | 8.52 | 4 | -0.22 | 0.03 | 4 | -16.6 |
| 683 | ESCULETIN | 305-01-1 | C9H6O4 | 178.15 | antifungal | p1 2-4 | -23.80 | 3.13 | 4 | 0.21 | 0.14 | 4 | 13.5 |
| 684 | 2',5'-DIHYDROXY-4-METHOXYCHALCONE | 6342-92-3 | C16H14O4 | 270.29 | 0 | p5 2-3 | -23.93 | 5.92 | 4 | -0.46 | 0.08 | 4 | -37.7 |
| 685 | METHYL TRIMETHOXYCINNAMATE | 7560-49-8, 20329-96-8 | C13H16O5 | 252.27 | 0 | p6 5-1 | -24.35 | 9.66 | 4 | 0.04 | 0.03 | 4 | 2.8 |
| 686 | KOBUSONE | 24173-71-5 | C14H22O2 | 222.33 | 0 | p1 2-8 | -24.42 | 17.62 | 4 | 0.01 | 0.10 | 4 | 0.5 |
| 687 | DOCONEXENT | 6217-54-5 | C22H32O2 | 328.50 | PAF inhibitor | p6 7-5 | -24.46 | 18.07 | 4 | -0.06 | 0.05 | 4 | -4.0 |
| 688 | DEHYDROCHOLIC ACID | 81-23-2 | C24H34O5 | 402.54 | choleretic | p10 9-5 | -24.47 | 17.89 | 4 | -0.06 | 0.03 | 4 | -4.2 |
| 689 | CHLOROGENIC ACID | 327-97-9 | C16H18O9 | 354.32 | antioxidant, free radical scavenger | p9 2-3 | -24.50 | 8.41 | 4 | -0.13 | 0.02 | 4 | -9.1 |
| 690 | TRIPTOPHENOLIDE | 74285-86-2 | C20H24O3 | 312.41 | 0 | p9 6-5 | -24.54 | 10.22 | 4 | -0.29 | 0.16 | 4 | -22.1 |
| 691 | 2-METHOXY-5 (6)EPOXY-TETRAHYDROCARYOPHYLLENE | 0 | C16H28O2 | 252.40 | 0 | p3 9-1 | -24.74 | 6.54 | 4 | -0.15 | 0.05 | 4 | -11.1 |
| 692 | CARMINIC ACID | 1260-17-9 | C22H20O14 | 508.40 | 0 | p5 8-2 | -24.88 | 10.47 | 4 | -0.10 | 0.11 | 4 | -7.5 |
| 693 | 7-OXOCHOLESTERYL ACETATE | 0 | C29H46O3 | 442.69 | 0 | p6 2-4 | -24.94 | 4.48 | 4 | -0.20 | 0.04 | 4 | -15.2 |
| 694 | PHLORACETOPHENONE | 480-66-0 | C8H8O4 | 168.15 | 0 | P2 7-3 | -25.30 | 8.69 | 4 | 0.44 | 0.24 | 3 | 26.5 |
| 695 | ARTHONIOIC ACID | 25556-24-5 | C29H36O9 | 528.60 | 0 | p3 4-2 | -25.37 | 14.37 | 4 | 0.02 | 0.09 | 4 | 1.1 |
| 696 | SOLANESOL | 13190-97-1 | C45H74O | 631.09 | 0 | p5 10-4 | -25.87 | 1.79 | 4 | 0.16 | 0.12 | 4 | 10.5 |
| 697 | GENETICIN | 49863-47-0, 108321-42-2(sulfate) | C20H40N4O10 | 496.56 | antibacterial | p5 9-4 | -26.05 | 16.30 | 4 | 0.07 | 0.07 | 4 | 4.9 |
| 698 | RIBOFLAVIN | 83-88-5 | C17H20N4O6 | 376.37 | Vitamin B2; Vitamin cofactor; LD50(rat) 560 mg/kg ip | p6 9-7 | -26.60 | 14.48 | 4 | 0.02 | 0.03 | 4 | 1.1 |
| 699 | HAEMATOXYLIN PENTAACETATE | 0 | C26H24O12 | 528.47 | 0 | p5 7-4 | -26.73 | 11.62 | 4 | 0.19 | 0.12 | 4 | 12.3 |
| 700 | CHOLESTEROL | 57-88-5 | C27H46O | 386.67 | emulsifying agent | p7 4-2 | -26.79 | 5.06 | 4 | -0.05 | 0.03 | 4 | -3.8 |
| 701 | IRIGINOL HEXAACETATE | 0 | C27H22O14 | 570.47 | 0 | p4 4-2 | -26.79 | 5.06 | 4 | -0.17 | 0.03 | 4 | -12.3 |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 702 | ACETOSYRINGONE | 2478-38-8 | C10H12O4 | 196.20 | insect attractant, plant hormone | p7 4-4 | -26.85 | 11.01 | 4 | -0.06 | 0.07 | 4 | -4.0 |
| 703 | ANGOLENSIN (R) | 4842-48-2 | C16H16O4 | 272.30 | 0 | p4 4-4 | -26.85 | 11.01 | 4 | -0.17 | 0.07 | 4 | -12.5 |
| 704 | DUARTIN (-) | 52305-04-1 | C18H20O6 | 332.36 | 0 | p5 6-3 | -26.87 | 16.43 | 4 | -0.20 | 0.09 | 4 | -15.3 |
| 705 | DIMETHYLCAFFEIC ACID | 14737-89-4 | C11H12O4 | 208.22 | 0 | p2 2-4 | -27.15 | 4.30 | 4 | -0.49 | 0.57 | 4 | -40.0 |
| 706 | EPINEPHRINE BITARTRATE | 51-42-3 | C13H19NO9 | 333.30 | adrenergic agonist, bronchodilator, antiglaucoma agent | p8 3-1 | -27.15 | 4.27 | 4 | 0.04 | 0.08 | 4 | 2.6 |
| 707 | HAEMATOXYLIN | 517-28-2 | C16H14O6 | 302.29 | 0 | p4 9-4 | -27.24 | 2.78 | 4 | 0.00 | 0.03 | 4 | 0.1 |
| 708 | TYRAMINE | 51-67-2 | C8H11NO | 137.18 | adrenergic agonist | p8 3-3 | -27.42 | 13.79 | 4 | -0.27 | 0.15 | 4 | -20.9 |
| 709 | 4-METHYLIMIDAZOLE | 822-36-6 | C4H6N2 | 82.11 | 0 | p6 3-2 | -27.80 | 13.76 | 4 | 0.18 | 0.07 | 4 | 11.5 |
| 710 | 5alpha-CHOLESTAN-3beta-OL-6-ONE | 0 | C27H46O2 | 402.67 | 0 | p2 1-6 | -27.83 | 14.93 | 4 | 0.53 | 0.04 | 4 | 30.6 |
| 711 | CADIN-4-EN-10-OL | 0 | C15H26O | 222.37 | 0 | p9 1-3 | -28.21 | 9.30 | 4 | -0.42 | 0.11 | 4 | -34.1 |
| 712 | SOLASODINE | 126-17-0 | C27H43NO2 | 413.65 | antineoplastic, antiinflammatory | p3 10-4 | -28.34 | 3.86 | 4 | 0.07 | 0.08 | 4 | 4.6 |
| 713 | 4-METHOXYDALBERGIONE | 4646-86-0 | C16H14O3 | 254.29 | 0 | p1 10-8 | -28.49 | 14.51 | 4 | -0.03 | 0.11 | 4 | -2.3 |
| 714 | APHYLLIC ACID | 642-67-1 | C15H26N2O2 | 266.39 | 0 | p1 10-7 | -28.53 | 19.92 | 4 | 0.25 | 0.03 | 4 | 16.1 |
| 715 | CARYLOPHYLLENE OXIDE | 1139-30-6 | C14H22O | 206.33 | 0 | p1 8-7 | -28.53 | 19.92 | 4 | -0.23 | 0.10 | 4 | -17.5 |
| 716 | BOLDINE | 476-70-0 | C19H21NO4 | 327.38 | 0 | p9 1-2 | -28.61 | 6.78 | 4 | -0.34 | 0.12 | 4 | -26.4 |
| 717 | ERGOSTEROL | 57-87-4 | C28H44O | 396.66 | 0 | p4 10-2 | -29.64 | 1.95 | 4 | -0.03 | 0.07 | 4 | -1.9 |
| 718 | TRIGONELLINE | 535-83-1 | C7H7NO2 | 137.14 | antihyperglycemic | P2 8-2 | -29.89 | 12.83 | 4 | 0.03 | 0.06 | 4 | 2.2 |
| 719 | PILOCARPINE NITRATE | 148-72-1, 92-13-7 [pilocarpine] | C11H17N3O5 | 271.28 | antiglaucoma agent, miotic | p10 10-2 | -30.24 | 2.97 | 4 | -0.10 | 0.03 | 4 | -7.3 |
| 720 | HUMULENE (alpha) | 6753-98-6 | C15H24 | 204.36 | 0 | p6 10-2 | -30.91 | 4.06 | 4 | 0.00 | 0.03 | 4 | 0.1 |
| 721 | GENTAMICIN SULFATE | 1405-41-0, 1403-66-3 [gentamicin] | C21H45N5O11S | 575.68 | antibacterial | p10 2-2 | -30.99 | 4.60 | 4 | -0.07 | 0.07 | 4 | -4.7 |
| 722 | RHETSININE | 526-43-2 | C19H17N3O2 | 319.37 | 0 | p2 6-1 | -31.21 | 10.59 | 4 | 0.51 | 0.23 | 4 | 29.6 |
| 723 | 13-METHYL-4,4-BISNOR-8,11,13-PODOCARPATRIEN-3-ONE | 0 | C16H20O | 228.34 | 0 | p8 1-6 | -31.37 | 15.11 | 4 | -0.03 | 0.10 | 4 | -2.0 |
| 724 | HARMALINE | 304-21-2 | C13H14N2O | 214.27 | CNS stimulant, antiparkinsonian agent | p6 5-2 | -31.87 | 10.11 | 4 | 0.01 | 0.03 | 4 | 0.9 |
| 725 | DIHYDROXY (3alpha,12alpha)PREGNAN-20-ONE | 0 | C21H34O3 | 334.50 | 0 | p8 9-5 | -32.59 | 19.91 | 4 | -0.37 | 0.05 | 4 | -29.0 |
| 726 | GUAIACOL | 90-05-1 | C7H8O2 | 124.14 | expectorant | p6 10-3 | -32.94 | 10.42 | 4 | 0.02 | 0.04 | 4 | 1.6 |
| 727 | ISOKOBUSONE | 24173-72-6 | C14H22O2 | 222.33 | 0 | p3 10-2 | -33.53 | 3.68 | 4 | -0.25 | 0.04 | 4 | -18.7 |
| 728 | SORBITOL | 50-70-4 | C6H14O6 | 182.17 | sweetening agent and humectant | p6 3-4 | -33.80 | 11.82 | 4 | -0.18 | 0.06 | 4 | -13.2 |
| 729 | 4,4'-DIMETHOXYDALBERGIONE | 0 | C17H16O4 | 284.31 | 0 | p5 6-4 | -34.16 | 35.02 | 4 | -0.01 | 0.08 | 4 | -0.7 |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 730 | POMIFERIN TRIMETHYL ETHER | 0 | C28H30O6 | 462.55 | derivative | p9 9-3 | -34.33 | 10.46 | 4 | 0.17 | 0.06 | 4 | 11.4 |
| 731 | METHYL ORSELLINATE | 3187-58-4 | C9H10O4 | 182.18 | 0 | p2 3-4 | -34.82 | 13.79 | 4 | 0.31 | 0.07 | 4 | 19.6 |
| 732 | beta-CAROTENE | 7235-40-7 | C40H56 | 536.89 | antioxidant; provitamin A | p7 10-2 | -34.82 | 5.87 | 4 | 0.04 | 0.07 | 4 | 2.8 |
| 733 | BISPHENOL A | 80-05-7 | C15H16O2 | 228.29 | endocrine disruptor, plastic monomer | p7 3-2 | -35.16 | 16.89 | 4 | -0.20 | 0.03 | 4 | -15.0 |
| 734 | DEACETOXY(7)-7-OXOKHIVORINIC ACID | 0 | C27H36O10 | 520.58 | 0 | p4 3-2 | -35.16 | 16.89 | 4 | -0.32 | 0.03 | 4 | -24.4 |
| 735 | NEROLIDOL | 7212-44-4 | C15H26O | 222.37 | 0 | p5 3-7 | -35.53 | 12.65 | 4 | -0.17 | 0.16 | 4 | -12.9 |
| 736 | ACETYL HYMETOCHROME | 2747-05-9 | C12H10O4 | 218.21 | 0 | p6 2-2 | -35.81 | 14.76 | 4 | -0.06 | 0.10 | 4 | -4.5 |
| 737 | RIBOSTAMYCIN SULFATE | 25546-65-0 | C17H36N4O14S | 552.56 | antibacterial | p9 5-2 | -35.94 | 13.39 | 4 | -0.03 | 0.23 | 4 | -2.0 |
| 738 | EPIANDROSTERONE | 0 | C19H30O2 | 290.45 | 0 | p3 4-1 | -36.02 | 4.97 | 4 | -0.05 | 0.02 | 4 | -3.8 |
| 739 | CHOLESTAN-3-ONE | 566-88-1 | C27H46O | 386.67 | 0 | p5 2-6 | -36.69 | 3.48 | 4 | -0.48 | 0.06 | 4 | -39.9 |
| 740 | PURPURIN | 81-54-9 | C14H8O5 | 256.22 | xanthin oxidase inhibitor, irritant | p3 7-3 | -37.23 | 5.62 | 4 | -0.19 | 0.02 | 4 | -14.3 |
| 741 | 3,4-DIDESMETHYL-5-DESHYDROXY-3'-ETHOXYSCLEROIN | 0 | C15H14O5 | 274.28 | 0 | p9 5-1 | -37.23 | 10.14 | 4 | -0.39 | 0.13 | 4 | -31.4 |
| 742 | RESVERATROL 4'-METHYL ETHER | 33626-08-3 | C15H14O3 | 242.28 | 0 | p7 2-2 | -37.33 | 11.06 | 4 | -0.37 | 0.07 | 4 | -29.0 |
| 743 | FRAXIDIN METHYL ETHER | 0 | C12H12O5 | 236.23 | 0 | p4 2-2 | -37.33 | 11.06 | 4 | -0.48 | 0.07 | 4 | -39.5 |
| 744 | CHOLEST-5-EN-3-ONE | 601-54-7 | C27H44O | 384.65 | 0 | p9 4-2 | -37.48 | 6.58 | 4 | 0.04 | 0.04 | 4 | 2.7 |
| 745 | APIGENIN DIMETHYL ETHER | 5728-44-9 | C17H14O5 | 298.30 | 0 | p1 2-3 | -37.84 | 16.95 | 4 | 0.17 | 0.16 | 4 | 11.3 |
| 746 | beta-AMYRIN | 559-70-6 | C30H50O | 426.73 | 0 | p9 10-2 | -38.19 | 9.19 | 4 | -0.12 | 0.12 | 4 | -8.3 |
| 747 | GUAIAZULENE | 489-84-9 | C15H18 | 198.31 | antioxidant, inhibits lipid peroxidation inhibitor, antiinflammatory, hepatoprotectant; LD50(rat) 1550 mg/kg po | p8 6-3 | -38.21 | 55.45 | 4 | -0.34 | 0.16 | 4 | -27.0 |
| 748 | DEHYDROROTENONE | 30990-44-4 | C23H20O6 | 392.41 | 0 | p5 5-3 | -38.48 | 8.13 | 4 | -0.07 | 0.08 | 4 | -4.9 |
| 749 | QUEBRACHITOL | 642-38-6 | C7H14O6 | 194.19 | 0 | p9 3-2 | -39.02 | 2.63 | 4 | -0.16 | 0.06 | 4 | -11.4 |
| 750 | 3-HYDROXYCOUMARIN | 939-19-5 | C9H6O3 | 162.15 | 0 | p3 10-3 | -39.59 | 7.07 | 4 | -0.21 | 0.03 | 4 | -15.7 |
| 751 | DEOXYCHOLIC ACID | 88-44-3 | C24H40O4 | 392.58 | 0 | p1 9-7 | -39.82 | 12.56 | 4 | 0.55 | 0.28 | 4 | 31.7 |
| 752 | FISSINOLIDE | 1915-69-1 | C29H36O8 | 512.61 | 0 | p1 7-7 | -39.82 | 12.56 | 4 | -0.81 | 0.06 | 4 | -75.3 |
| 753 | 3-ACETYLGEDUNOL | 0 | C30H40O8 | 528.65 | 0 | p1 5-7 | -40.49 | 7.59 | 4 | 1.19 | 0.12 | 3 | 56.3 |
| 754 | 21-ACETOXYPREGNENOLONE | 566-78-9 | C23H34O4 | 374.53 | precursor in corticoid biosynthesis, derivative | p5 8-5 | -41.17 | 5.68 | 4 | 0.10 | 0.10 | 4 | 6.5 |
| 755 | URSODIOL | 128-13-2 | C24H40O4 | 392.58 | anticholelithogenic; LD50(rat) 890 mg/kg ip | p10 10-3 | -41.66 | 8.38 | 4 | -0.15 | 0.05 | 4 | -10.9 |
| 756 | HARPAGOSIDE | 19210-12-9 | C23H28O11 | 480.47 | 0 | p5 9-5 | -42.12 | 2.29 | 4 | 0.36 | 0.09 | 4 | 21.8 |
| 757 | ORNITHINE HYDROCHLORIDE | 70-26-8 | C5H13ClN2O2 | 168.62 | hepatoprotectant, anticholesteremic | p6 10-5 | -42.36 | 8.44 | 4 | -0.07 | 0.12 | 4 | -5.2 |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 758 | ALIZARIN | 72-48-0 | C14H8O4 | 240.22 | antimutagen | p9 5-3 | -42.36 | 4.93 | 4 | -0.13 | 0.07 | 4 | -9.1 |
| 759 | KINETIN | 525-79-1 | C10H9N5O | 215.22 | auxin, plant growth regulator, plant cell division promotor | p1 6-4 | -42.74 | 18.96 | 4 | 0.54 | 0.02 | 4 | 31.0 |
| 760 | CITROPTEN | 487-06-9 | C11H10O4 | 206.20 | photosensitizing agent | p2 6-2 | -43.58 | 6.75 | 4 | 0.38 | 0.07 | 4 | 23.1 |
| 761 | 2,3,4-TRIHYDROXY-4'-ETHOXYBENZOPHENONE | 0 | C15H14O5 | 274.28 | 0 | p9 10-8 | -43.73 | 7.79 | 4 | 0.22 | 0.05 | 4 | 14.4 |
| 762 | GRAMINE | 87-52-5 | C11H14N2 | 174.25 | 0 | p8 7-4 | -43.87 | 19.34 | 4 | -0.42 | 0.13 | 4 | -33.5 |
| 763 | APIGENIN | 520-36-5 | C15H10O5 | 270.24 | antispasmodic, antineoplastic, topoisomerase I inhibitor | p9 10-3 | -44.57 | 6.62 | 4 | 0.06 | 0.05 | 4 | 3.9 |
| 764 | METHYL ROBUSTONE | 0 | C22H18O6 | 378.39 | 0 | P2 9-5 | -44.64 | 13.43 | 4 | -0.08 | 0.15 | 4 | -5.4 |
| 765 | CITRULLINE | 627-77-0 | C6H13N3O3 | 175.19 | 0 | p1 5-4 | -44.68 | 15.25 | 4 | 0.62 | 0.10 | 2 | 34.9 |
| 766 | ATRANORIN | 479-20-9 | C19H18O8 | 374.35 | 0 | p1 4-7 | -45.91 | 11.98 | 4 | 1.02 | 0.16 | 4 | 50.7 |
| 767 | LAWSONE | 83-72-7 | C10H6O3 | 174.16 | 0 | p6 1-5 | -46.08 | 13.52 | 4 | -0.16 | 0.11 | 4 | -12.0 |
| 768 | PYRROMYCIN | 668-17-7 | C30H35NO11 | 585.61 | antibacterial | p8 3-5 | -46.08 | 5.01 | 4 | 0.35 | 0.15 | 4 | 21.5 |
| 769 | DEFEROXAMINE MESYLATE | 138-14-7, 70-51-9 [deferoxamine] | C26H52N6O11S | 656.80 | chelating agent (Fe & Al) | p10 3-1 | -48.55 | 15.61 | 4 | 0.31 | 0.07 | 4 | 19.6 |
| 770 | LATHOSTEROL | 0 | C27H46O | 386.67 | 0 | p2 3-8 | -50.10 | 20.42 | 4 | 0.35 | 0.08 | 4 | 21.4 |
| 771 | HYDROXYPROGESTERONE | 3168-01-2 | C21H30O3 | 330.47 | progestin | p6 9-4 | -50.17 | 0.99 | 4 | 0.37 | 0.06 | 4 | 22.7 |
| 772 | APIOLE | 523-80-8 | C12H14O4 | 222.24 | antipyretic, diuretic, insecticide | p7 5-4 | -50.23 | 2.73 | 4 | 0.06 | 0.04 | 4 | 3.8 |
| 773 | 3alpha-HYDROXY-4,4-BISNOR-8,11,13-PODOCARPATRIENE | 0 | C15H20O | 216.33 | 0 | p4 5-4 | -50.23 | 2.73 | 4 | -0.06 | 0.04 | 4 | -4.1 |
| 774 | GARCINOLIC ACID | 0 | C38H46O9 | 646.78 | 0 | p2 3-2 | -51.29 | 18.22 | 4 | 0.36 | 0.16 | 4 | 22.0 |
| 775 | NOSCAPINE HYDROCHLORIDE | 912-60-7, 128-62-1 [noscapine] | C22H24ClNO7 | 449.89 | antitussive | p10 2-4 | -51.62 | 13.18 | 4 | 0.30 | 0.05 | 4 | 18.9 |
| 776 | EPICATECHIN PENTAACETATE | 0 | C25H24O11 | 500.46 | 0 | p6 3-1 | -52.46 | 17.01 | 4 | -0.02 | 0.01 | 4 | -1.3 |
| 777 | ALLOPREGNANOLONE | 0 | C21H34O2 | 318.50 | 0 | p4 9-1 | -52.47 | 4.62 | 4 | 0.02 | 0.08 | 4 | 1.3 |
| 778 | EQUILIN | 474-86-2 | C18H20O2 | 268.36 | estrogen | p10 6-1 | -53.61 | 45.92 | 4 | -0.60 | 0.10 | 4 | -51.5 |
| 779 | CAPSAICIN | 404-86-4 | C18H27NO3 | 305.42 | analgesic (topical), depletes Substance P, neurotoxic | p10 1-4 | -54.23 | 9.61 | 4 | 0.00 | 0.17 | 4 | 0.1 |
| 780 | THEANINE POTASSIUM | 3081-61-6 | C7H13KN2O3 | 212.30 | 0 | p3 5-3 | -54.47 | 14.26 | 4 | -0.45 | 0.07 | 4 | -36.3 |
| 781 | HARMOL HYDROCHLORIDE | 40580-83-4 | C12H11ClN2O | 234.69 | MAO inhibitor | p1 2-2 | -55.14 | 10.17 | 4 | -0.14 | 0.05 | 4 | -10.1 |
| 782 | LITHOCHOLIC ACID | 434-13-9 | C24H40O3 | 376.58 | LD50(mouse) 3900 mg/kg po | p1 2-5 | -55.75 | 9.37 | 4 | 0.65 | 0.06 | 4 | 36.1 |
| 783 | JUAREZIC ACID | 1552-94-9 | C11H10O2 | 174.20 | 0 | p3 5-2 | -55.89 | 17.98 | 4 | -0.57 | 0.05 | 4 | -48.4 |
| 784 | PHYSCION | 521-61-9 | C16H12O5 | 284.27 | antibacterial, cathartic | p9 9-5 | -57.45 | 5.78 | 4 | 0.20 | 0.03 | 4 | 12.9 |
| 785 | ABIETIC ACID | 514-10-3 | C20H30O2 | 302.46 | 0 | p9 2-2 | -58.27 | 13.29 | 4 | -0.39 | 0.11 | 4 | -30.7 |

| | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 786 | GLYCOCHOLIC ACID | 475-31-0 | C26H43NO6 | 465.64 | 0 | p8 6-4 | -58.36 | 28.23 | 4 | -0.31 | 0.30 | 4 | -23.7 |
| 787 | POMIFERIN DIMETHYL ETHER | 0 | C27H28O6 | 448.52 | 0 | p9 4-3 | -58.61 | 11.00 | 4 | 0.09 | 0.06 | 4 | 6.1 |
| 788 | CORYNANTHINE | 123333-62-0 | C21H26N2O3 | 354.45 | 0 | p8 7-7 | -58.95 | 29.94 | 4 | -0.61 | 0.06 | 4 | -53.1 |
| 789 | MELATONIN | 73-31-4 | C13H16N2O2 | 232.28 | sleep induction, modifies circadian rhythm | p2 2-7 | -62.19 | 3.45 | 4 | -1.56 | 0.66 | 4 | -195.5 |
| 790 | TRIACETYLRESVERATROL | 42206-94-0 | C20H18O6 | 354.36 | 0 | p3 4-3 | -64.78 | 13.82 | 4 | 0.19 | 0.12 | 4 | 12.4 |
| 791 | 3-METHOXYCATECHOL | 934-00-9 | C7H8O3 | 140.14 | 0 | p3 8-2 | -66.69 | 9.30 | 4 | 0.05 | 0.04 | 4 | 3.2 |
| 792 | CHRYSOPHANOL | 481-74-3 | C15H10O4 | 254.24 | 0 | P2 9-4 | -71.62 | 13.37 | 4 | 0.17 | 0.16 | 4 | 11.4 |
| 793 | UBIDECARENEONE | 303-98-0 | C59H90O4 | 863.37 | cardiovascular agent | p1 10-5 | -74.78 | 16.33 | 4 | 0.35 | 0.15 | 4 | 21.3 |
| 794 | 7-DEACETYLKHIVORIN | 0 | C30H40O9 | 544.65 | 0 | p1 8-5 | -74.78 | 16.33 | 4 | -0.55 | 0.06 | 4 | -46.2 |
| 795 | VULPINIC ACID | 521-52-8 | C19H14O5 | 322.32 | antiinflammatory, antibacterial, plant growth inhibitor | p7 10-4 | -77.92 | 7.79 | 4 | 0.64 | 0.09 | 4 | 36.0 |
| 796 | FUSIDIC ACID | 6990-06-3 | C31H48O6 | 516.72 | antibacterial | p10 1-2 | -82.83 | 11.31 | 4 | -0.30 | 0.14 | 4 | -23.2 |
| 797 | SINOMENINE | 115-53-7 | C19H23NO4 | 329.40 | weak abortifacient, immunosuppressant, analgesic, antiinflammatory; LD50 (po) 580 mg/kg; (ip) 285 mg/kg(mouse) | p2 2-8 | -83.45 | 48.85 | 4 | -0.78 | 0.59 | 4 | -71.8 |
| 798 | QUERCETIN 5,7,3',4'-TETRAMETHYL ETHER | 1244-78-6 | C19H18O7 | 358.35 | 0 | p8 7-3 | -84.09 | 21.55 | 4 | -0.81 | 0.33 | 4 | -75.6 |
| 799 | TANSHINONE IIA SULFONATE SODIUM | 0 | C19H17NaO6S | 396.40 | free radical scavenger | p7 3-3 | -96.29 | 8.40 | 4 | 0.01 | 0.04 | 4 | 0.9 |
| 800 | HETEROPEUCENIN, METHYL ETHER | 26213-95-6 | C16H18O4 | 274.32 | 0 | p4 3-3 | -96.29 | 8.40 | 4 | -0.10 | 0.04 | 4 | -7.2 |
| 790 | TRIACETYLRESVERATROL | 42206-94-0 | C20H18O6 | 354.36 | 0 | p3 4-3 | -64.78 | 13.82 | 4 | 0.19 | 0.12 | 4 | 12.4 |
| 791 | 3-METHOXYCATECHOL | 934-00-9 | C7H8O3 | 140.14 | 0 | p3 8-2 | -66.69 | 9.30 | 4 | 0.05 | 0.04 | 4 | 3.2 |
| 792 | CHRYSOPHANOL | 481-74-3 | C15H10O4 | 254.24 | 0 | P2 9-4 | -71.62 | 13.37 | 4 | 0.17 | 0.16 | 4 | 11.4 |
| 793 | UBIDECARENEONE | 303-98-0 | C59H90O4 | 863.37 | cardiovascular agent | p1 10-5 | -74.78 | 16.33 | 4 | 0.35 | 0.15 | 4 | 21.3 |
| 794 | 7-DEACETYLKHIVORIN | 0 | C30H40O9 | 544.65 | 0 | p1 8-5 | -74.78 | 16.33 | 4 | -0.55 | 0.06 | 4 | -46.2 |
| 795 | VULPINIC ACID | 521-52-8 | C19H14O5 | 322.32 | antiinflammatory, antibacterial, plant growth inhibitor | p7 10-4 | -77.92 | 7.79 | 4 | 0.64 | 0.09 | 4 | 36.0 |
| 796 | FUSIDIC ACID | 6990-06-3 | C31H48O6 | 516.72 | antibacterial | p10 1-2 | -82.83 | 11.31 | 4 | -0.30 | 0.14 | 4 | -23.2 |
| 797 | SINOMENINE | 115-53-7 | C19H23NO4 | 329.40 | weak abortifacient, immunosuppressant, analgesic, antiinflammatory; LD50 (po) 580 mg/kg; (ip) 285 mg/kg(mouse) | p2 2-8 | -83.45 | 48.85 | 4 | -0.78 | 0.59 | 4 | -71.8 |
| 798 | QUERCETIN 5,7,3',4'-TETRAMETHYL ETHER | 1244-78-6 | C19H18O7 | 358.35 | 0 | p8 7-3 | -84.09 | 21.55 | 4 | -0.81 | 0.33 | 4 | -75.6 |
| 799 | TANSHINONE IIA SULFONATE SODIUM | 0 | C19H17NaO6S | 396.40 | free radical scavenger | p7 3-3 | -96.29 | 8.40 | 4 | 0.01 | 0.04 | 4 | 0.9 |
| 800 | HETEROPEUCENIN, METHYL ETHER | 26213-95-6 | C16H18O4 | 274.32 | 0 | p4 3-3 | -96.29 | 8.40 | 4 | -0.10 | 0.04 | 4 | -7.2 |

**Table A-2 Secondary screening: Anti-cryptosporidial activity of 88 compounds at 3.3 uM.**

| # | Compound | CAS # | Formula | Mol Wt | Bioactivity and note | Plate # | % Inhibition (3.3 uM) | SEM | N |
|---|---|---|---|---|---|---|---|---|---|
| **1** | MONENSIN SODIUM (monensin A is shown) | 22373-78-0, 17090-79-8 (monensin) | C37H63NaO10 | 690.89846 | antibacterial | P10 6-6 | 98.54 | 0.225 | 4 |
| **2** | DACTINOMYCIN | 50-76-0 | C62H86N12O16 | 1255.44752 | antineoplastic, intercalating agent | P6 10-6 | 96.68 | 0.594 | 4 |
| **3** | EMETINE DIHYDROCHLORIDE | 316-42-7, 483-18-1 [emetine] | C29H42Cl2N2O4 | 553.57509 | inhibits RNA, DNA and protein synthesis | P2 1-4 | 94.63 | 0.752 | 4 |
| **4** | PACLITAXEL | 33069-62-4 | C47H51NO14 | 853.92882 | antineoplastic | P10 2-7 | 92.53 | 0.563 | 4 |
| **5** | CHRYSANTHEMIC ACID, ETHYL ESTER | 0 | C12H20O2 | 196.292 | insecticide | P1 6-1 | 90.52 | 1.719 | 4 |
| **6** | VALINOMYCIN | 2001-95-8 | C54H90N6O18 | 1111.3488 | antibiotic; LD50 (rat, po) 4 mg/kg | P7 4-1 | 87.39 | 2.064 | 4 |
| **7** | MITOMYCIN | 50-07-7 | C15H18N4O5 | 334.33451 | antineoplastic | P7 9-2 | 78.37 | 2.139 | 4 |
| **8** | CYCLOSPORINE | 59865-13-3 | C62H111N11O12 | 1202.64247 | immunosuppressant | p10 2-6 | 77.48 | 0.946 | 4 |
| **9** | DEACETOXY-7-OXOGEDUNIN | 0 | C26H30O6 | 438.5254 | 0 | p3 8-8 | 77.27 | 3.503 | 4 |
| **10** | ROTENONE | 83-79-4 | C23H22O6 | 394.42819 | acaricide, ectoparasiticide, antineoplastic, mitochondrial poison | P8 5-5 | 76.20 | 3.381 | 4 |
| **11** | DIHYDROTANSHINONE I | 0 | C18H14O3 | 278.31048 | 0 | p5 7-6 | 75.35 | 8.448 | 4 |
| **12** | 3-DEOXO-3beta-HYDROXYMEXICANOLIDE 16-ENOL ETHER | 0 | C28H36O7 | 484.59492 | 0 | P4 6-1 | 71.17 | 3.016 | 4 |
| **13** | DEOXYSAPPANONE B 7,3'-DIMETHYL ETHER ACETATE | 0 | C20H20O6 | 356.3788 | 0 | p5 4-4 | 70.78 | 3.559 | 4 |
| **14** | DAUNORUBICIN | 20830-81-3 | C27H29NO10 | 527.53288 | antineoplastic | p10 2-1 | 70.55 | 4.883 | 4 |
| **15** | DIGOXIGENIN | 1672-46-4 | C23H34O5 | 390.52443 | 0 | P3 6-5 | 69.00 | 1.396 | 4 |
| **16** | VINBLASTINE SULFATE | 143-67-9, 865-21-4 [vinblastine] | C46H60N4O13S | 909.0741 | antineoplastic, spindle poison | p6 2-7 | 67.20 | 6.711 | 4 |
| **17** | BAICALEIN | 491-67-8 | C15H10O5 | 270.24395 | antiviral (HIV) | p3 3-3 | 66.47 | 2.223 | 4 |
| **18** | PODOPHYLLIN ACETATE | 1180-34-3 | C24H24O9 | 456.45348 | 0 | p5 3-6 | 64.16 | 5.289 | 4 |
| **19** | 8beta-HYDROXYCARAPIN, 3,8-HEMIACETAL | 0 | C27H32O8 | 484.55129 | 0 | P3 5-7 | 63.66 | 3.157 | 4 |
| **20** | TANSHINONE IIA | 568-72-9 | C19H18O3 | 294.35351 | antineoplastic, bone resorption inhibitor, antiproliferative, apoptosis inducer | P8 4-4 | 62.56 | 2.870 | 4 |
| **21** | DIMETHYLSULFONE | 67-71-0 | C2H6O2S | 94.13292 | antiinflammatory, antiproliferative, antiparasitic | p7 8-3 | 61.42 | 8.343 | 4 |
| **22** | CAMPTOTHECIN | 7689-03-4 | C20H16N2O4 | 348.36152 | antineoplastic | p5 5-7 | 58.81 | 3.040 | 4 |
| **23** | 2,3,4'-TRIHYDROXY-4-METHOXYBENZOPHENONE | 0 | C14H12O5 | 260.24874 | 0 | p5 10-2 | 58.62 | 7.864 | 4 |
| **24** | LOVASTATIN | 75330-75-5 | C24H36O5 | 404.55152 | antihyperlipidemic, HMGCoA reductase inhibitor | p2 1-3 | 58.15 | 3.064 | 4 |
| **25** | DIHYDROGAMBOGIC ACID | 0 | C38H46O8 | 630.78552 | 0 | P1 4-3 | 57.34 | 5.704 | 4 |
| **26** | PICROPODOPHYLLIN | 477-47-4 | C22H22O8 | 414.41584 | Insulin growth factor 1 receptor inhibitor, antineoplastic | p9 7-4 | 56.40 | 3.658 | 4 |
| **27** | DEACETYLGEDUNIN | 0 | C26H32O6 | 440.54134 | 0 | P4 10-6 | 55.53 | 5.999 | 4 |
| **28** | DEOXYSAPPANONE B 7,4'-DIMETHYL ETHER | 0 | C18H18O5 | 314.34116 | 0 | P4 8-6 | 51.85 | 5.615 | 4 |
| **29** | 3,16-DIDEOXYMEXICANOLIDE-3beta-DIOL | 0 | C27H36O7 | 472.58377 | 0 | p6 9-1 | 51.59 | 11.089 | 4 |
| **30** | DIMETHYL GAMBOGINATE | 0 | C40H49ClO8 | 693.28473 | 0 | P6 7-1 | 46.51 | 6.662 | 4 |
| **31** | ISOOSAJIN | 5745-54-0 | C25H24O5 | 404.46703 | 0 | P5 1-4 | 38.75 | 10.366 | 4 |
| **32** | HESPERIDIN | 520-26-3 | C28H34O15 | 610.57418 | capillary protectant | p7 7-8 | 36.06 | 11.290 | 4 |
| **33** | SIROLIMUS | 53123-88-9 | C51H79NO13 | 914.19718 | immunosuppressant, antineoplastic; rapamycin | p10 4-7 | 35.01 | 5.341 | 4 |
| **34** | BUSSEIN | 41060-14-4 | C43H54O18 | 858.89903 | 0 | P4 5-2 | 33.59 | 6.632 | 4 |
| **35** | HAEMATOPORPHYRIN | 14459-29-1 | C34H38N4O6 | 598.70516 | antidepressant, antineoplastic | P8 9-4 | 33.12 | 9.671 | 4 |
| **36** | PRISTIMERIN | 1258-84-0 | C30H40O4 | 464.6509 | antineoplastic, antiinflammatory | P3 8-5 | 30.25 | 8.129 | 4 |
| **37** | DEMETHYLNOBILETIN | 2174-59-6 | C20H20O8 | 388.3776 | 0 | P1 6-8 | 28.60 | 4.475 | 4 |
| **38** | ACETYL ISOGAMBOGIC ACID | 0 | C40H46O9 | 670.80722 | 0 | P3 7-5 | 27.42 | 6.351 | 4 |
| **39** | PHENYLALANIINE (L) HYDROCHLORIDE | 63-91-2(base) | C9H12ClNO2 | 201.65449 | amino acid | p10 5-5 | 25.58 | 7.799 | 4 |

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|---|---|---|---|---|---|---|---|---|---|
| **40** | 3alpha-ACETOXYDIHYDRODEOXYGEDUNIN | 0 | C30H40O7 | 512.6491 | 0 | P4 4-1 | 24.87 | 6.411 | 4 |
| **41** | TOMATINE | 86273-92-9 | C47H79NO21 | 994.14778 | antifungal, antibacterial, antiinflammatory agent | P9 3-6 | 24.76 | 9.904 | 4 |
| **42** | RESERPINE | 50-55-5 | C33H40N2O9 | 608.69475 | antihypertensive | P10 4-3 | 24.13 | 2.747 | 4 |
| **43** | beta-SITOSTEROL | 83-46-5 | C29H50O | 414.72125 | 0 | P8 8-5 | 20.34 | 8.928 | 4 |
| **44** | STROPHANTHIDINIC ACID LACTONE ACETATE | 0 | C25H32O7 | 444.52959 | 0 | P3 4-4 | 18.83 | 7.912 | 4 |
| **45** | URIDINE TRIPHOSPHATE TRISODIUM | 19817-92-6 | C9H12N2Na3O15P3 | 550.09119 | psychostimulant | P8 2-1 | 17.48 | 12.694 | 4 |
| **46** | TRYPTOPHAN | 73-22-3 ['L'] | C11H12N2O2 | 204.23049 | antidepressant, nutrient; LD50(rat) 1634 mg/kg ip | p1 7-6 | 16.82 | 2.939 | 4 |
| **47** | ESTRAGOLE | 140-67-0 | C10H12O | 148.20654 | insect atttractant, skin irritant, carcinogen | P8 2-4 | 15.45 | 6.831 | 4 |
| **48** | BENZYL ISOTHIOCYANATE | 622-78-6 | C8H7NS | 149.21569 | antineoplastic, antibacterial, antifungal | P9 1-8 | 13.78 | 9.025 | 4 |
| **49** | PLUMBAGIN | 481-42-5 | C11H8O3 | 188.18461 | antibacterial, antifungal, tuberculostatic; antifeedant (worm) | P5 10-5 | 13.49 | 4.047 | 4 |
| **50** | TRYPTAMINE | 61-54-1 | C10H12N2 | 160.22054 | psychotropic | P8 7-2 | 12.30 | 4.436 | 4 |
| **51** | PIPLARTINE | 20069-09-4 | C17H19NO5 | 317.34468 | anti-asthma, antibronchitis | p5 5-1 | 10.32 | 20.666 | 4 |
| **52** | PATULIN | 149-29-1 | C7H6O4 | 154.12347 | antibacterial | P9 10-4 | 9.51 | 8.797 | 4 |
| **53** | GRISEOFULVIN | 126-07-8 | C17H17ClO6 | 352.77444 | antifungal, inhibits mitosis in metaphase | p10 6-8 | 8.76 | 8.338 | 4 |
| **54** | SAFROLE | 94-59-7 | C10H10O2 | 162.19 | anesthetic (topical) and antiseptic, pediculicide | P9 3-8 | 7.95 | 16.159 | 4 |
| **55** | 3-HYDROXYTYRAMINE | 62-31-7 | C8H11NO2 | 153.18237 | dopaminergic | P1 9-6 | 5.87 | 7.112 | 4 |
| **56** | IVERMECTIN | 70288-86-7 | C48H74O14 | 875.11658 | antiparasitic | p10 1-8 | 5.64 | 9.338 | 4 |
| **57** | 1,3-DIDEACETYL-7-DEACETOXY-7-OXOKHIVORIN | 0 | C26H34O7 | 458.55668 | 0 | p3 7-4 | 3.03 | 16.462 | 4 |
| **58** | TETRANDRINE | 518-34-3 | C38H42N2O6 | 622.76824 | analgesic, antineoplastic, antihypertensive, lymphotoxin | P9 1-7 | 0.58 | 9.680 | 4 |
| **59** | RUTILANTINONE | 21288-61-9 | C22H20O9 | 428.3993 | coccidiostat | P9 2-6 | -3.37 | 8.361 | 4 |
| **60** | QUINIC ACID | 77-95-2 | C7H12O6 | 192.17009 | 0 | p7 6-8 | -6.44 | 12.672 | 4 |
| **61** | STIGMASTA-4,22-DIEN-3-ONE | 20817-72-5 | C29H46O | 410.68937 | 0 | p7 9-8 | -6.48 | 12.535 | 4 |
| **62** | OCTOPAMINE HYDROCHLORIDE | 104-14-3 | C8H12ClNO2 | 189.64334 | adrenergic agonist | P7 5-2 | -12.13 | 7.635 | 4 |
| **63** | TETRAHYDROGAMBOGIC ACID | 0 | C38H48O8 | 632.80146 | 0 | P9 2-8 | -12.49 | 9.599 | 4 |
| **64** | ERYTHROMYCIN | 114-07-8 | C37H67NO13 | 733.94544 | antibacterial | P6 2-8 | -13.37 | 10.965 | 4 |
| **65** | TACROLIMUS | 109581-93-3, 104987-11-3 [anhydrous] | C44H69NO12 | 804.04003 | immune suppressant, antifungal | p10 3-7 | -13.92 | 21.927 | 4 |
| **66** | ABAMECTIN (avermectin B1a shown) | 71751-41-2 | C48H72O14 | 873.10064 | antiparisitic | P8 3-6 | -19.06 | 7.038 | 4 |
| **67** | GLUTATHIONE | 70-18-8 | C10H17N3O6S | 307.32749 | antioxidant | P9 5-8 | -19.68 | 17.405 | 4 |
| **68** | 3beta-HYDROXYDEOXODIHYDRODEOXYGEDUNIN | 0 | C28H38O6 | 470.61146 | 0 | p4 7-4 | -21.43 | 22.230 | 4 |
| **70** | NOBILETIN | 478-01-3 | C21H22O8 | 402.40469 | matrix metaloproteinase inhibitor; antineoplastic | P5 7-1 | -24.68 | 17.261 | 4 |
| **71** | QUERCETIN | 117-39-5, 6151-25-3(hydrate) | C15H10O7 | 302.24275 | capillary protectant, antioxidant. antineoplastic, anti-HIV | P7 7-4 | -27.08 | 15.748 | 4 |
| **72** | 3-HYDROXYFLAVONE | 577-85-5 | C15H10O3 | 238.24515 | 0 | p8 3-8 | -27.76 | 8.035 | 4 |
| **73** | SILIBININ | 22888-70-6 | C25H22O10 | 482.44809 | hepatoprotective agent, antioxidant | P7 1-2 | -30.46 | 37.726 | 4 |
| **74** | HEXAMETHYLQUERCETAGETIN | 1251-84-9 | C21H22O8 | 402.40469 | 0 | P3 1-7 | -42.32 | 13.240 | 4 |
| **75** | MUNDULONE | 481-94-7 | C26H26O6 | 434.49352 | 0 | p4 10-4 | -43.37 | 18.514 | 4 |
| **76** | CAPREOMYCIN SULFATE | 1405-37-4, 11003-38-6 [capreomycin] | C25H46N14O12S | 766.79597 | antibacterial, tuberculostatic | P7 2-8 | -58.12 | 30.183 | 4 |
| **77** | HARMINE | 442-51-3 | C13H12N2O | 212.25339 | antiparkinsonian, CNS stimulant | p9 4-8 | -62.02 | 18.915 | 4 |
| **78** | DIHYDROCELASTROL | 0 | C29H40O4 | 452.63975 | 0 | P1 7-1 | -65.99 | 10.441 | 4 |
| **79** | CHRYSIN DIMETHYL ETHER | 21392-57-4 | C17H14O4 | 282.29873 | 0 | P8 8-6 | -68.90 | 15.080 | 4 |
| **80** | ASARYLALDEHYDE | 4460-86-0 | C10H12O4 | 196.20474 | fly attractant | P8 6-5 | -73.93 | 14.552 | 4 |
| **81** | DERRUSTONE | 2204-59-3 | C18H14O6 | 326.30868 | 0 | p7 6-7 | -76.91 | 35.569 | 4 |
| **82** | 5-HYDROXY-2',4',7,8-TETRAMETHOXYFLAVONE | 123316-61-0 | C19H18O7 | 358.35111 | 0 | P6 5-7 | -82.59 | 36.196 | 4 |
| **83** | CYCLOVERATRYLENE | 0 | C27H30O6 | 450.53655 | 0 | P8 1-5 | -85.33 | 51.067 | 4 |

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|---|---|---|---|---|---|---|---|---|---|
| **84** | AVERMECTIN A1a | 0 | C49H74O14 | 887.12773 | antiparasitic | P5 1-7 | -85.37 | 35.377 | 4 |
| **85** | CRYPTOTANSHINONE | 35825-57-1 | C19H20O3 | 296.36945 | inhibits angiogenesis | P4 2-8 | -85.47 | 9.616 | 4 |
| **86** | OBTUSAQUINONE | 21105-15-7 | C16H14O3 | 254.28818 | 0 | p4 6-5 | -91.76 | 40.908 | 4 |
| **87** | LAPACHOL | 84-79-7 | C15H14O3 | 242.27703 | antineoplastic, antifungal | P8 8-8 | -98.02 | 8.340 | 4 |
| **88** | 4-NONYLPHENOL | 104-40-5 | C15H24O | 220.35793 | weevil pheromone, shows estrogenic activity | p9 9-8 | -181.29 | 41.784 | 4 |