Plant derived antifungals- trends and potential applications in veterinary medicine: A mini-review

Nopamart Trakranrungsie
Department of Preclinical Sciences, Faculty of Veterinary Science, Mahidol University, Salaya, Nakhonpathom 73170, Thailand

Due to increasing resistance of fungi against conventional drugs, as well as the observable side effects of the already limited numbers of antifungals commonly used in veterinary practice, the fungal infections among animals, whether superficial or systemic, often pose substantial management problems and are still a major concern. In this regard, the alternative ‘herbal formulations’ have become a renewed interest. Medicinal plants are in fact an integral part of ethnoveterinary medicine and the practice is rather common in Asian countries, including China, India, Japan, Pakistan, Sri Lanka and Thailand. Development in information technology has facilitated an explosion in the range and content of electronic information concerning medicinal plants as a re-emergent health aid for both animals and humans. It has been estimated that more than 100,000 plants/plant extracts have been assayed for their pharmacological properties. Based on the current available data and the recently proposed IC<sub>50</sub> < 100 μg/ml or MIC < 500 μg/ml as a cut-off value if the extracts would possess any promising antifungal effect, the potential candidates are summarized with their reported major constituents. The indigenous plants with strong antifungal activity abundantly found in certain regions, the example of their herbal products and the efficacy testing are also presented.

Keywords antifungal; plant extract; Piper betle; dermatophytes

1. Introduction

Plants have always served as essential sources of therapeutic agents for humans and animals. Records of medicinal plants and their therapeutic values appear not only in the classic literature of traditional knowledge in all cultures of the East and West, but also in numerous recent publications and databases developed by several institutes and organizations such as the University of Illinois at Chicago (http://www.napralert.org/), Indian Institute of Ayurveda and Integrative Medicine (http://www.friht.org.in/), and Mahidol University (http://www.pharmacy.mahidol.ac.th/medplantdatabase/) [1-6]. The return of interest in pharmacologic activity of plants, plant extracts and isolated plant compounds in the past decades has markedly energized the establishment of standardized methods of preparation and extraction, as well as standard assays and criteria for activity, as parts of the process in drug discovery and development [7].

Traditionally, the herbal remedies may be offered more or less in a holistic approach for maintenance and well-being of health, enhanced various body processes, and some symptomatic relief. Although a cyclical phenomenon has been described as a pattern of interest in herbal medicine in veterinary practice, the modern herbal formulation based on scientific proven efficacy may provide a re-invented paradigm of treatment of choice for specific disease conditions with a stronger reliability and predictability of clinical outcomes [8, 9].

In animals, dermatophytic infections are often challenging to manage and some do pose zoonotic potential. The course of treatment particularly in companion animals requires long-term drug administration and hence is costly. The application of plant-derived antifungal compounds, i.e. as topical therapy, could be one of the attractive alternatives. This article provides an overview of fungal infections in animals and their clinical significance. The currently available conventional antifungals and their clinical limitations in veterinary practice are summarized. In addition, due to the renewed and increasing interest in the application of medicinal plants and plant-derived products as the treatment of choice observed in recent years, plants with promising antifungal activity with reported IC<sub>50</sub> (concentration inhibiting 50% of fungal growth) < 100 μg/ml or MIC (minimum concentration resulting in no visible fungal growth) < 500 μg/ml are listed exclusively. Finally, trends in herbal modalities and potential applications of plant-derived antifungals in veterinary medicine are discussed.

2. Fungal infection in animals and their clinical significance

Major fungal infections in animals can be recognized in the forms of both systemic and superficial infections. Several fungal species including Aspergillus spp., Cryptococcus neoformans, Histoplasma capsulatum and Candida spp. could be involved in the pathogenesis of systemic mycoses. The common causes of superficial mycoses, on the other hand, are dermatophytes, the keratinophilic fungi consisting of three genera: Microsporum, Trichophyton, and Epidermophyton. In companion animals, Microsporum canis, Microsporum gypseum and Trichophyton mentagrophytes are considered the main causative pathogens of skin infections, of which M. canis accounts for 50-70% and 90-98% of the identified cases in dogs and cats, respectively [10]. M. persicolor, M. verrucosum, T. terrestre, T.
rubrum, T. equinum, T. schoenleineee and E. floccosum can also be isolated from the animal skin, however, their clinical significance is limited [11].

Fungal infections among animals are and will still be a major concern not only for veterinary but also public health. In most cases, treatment of clinical mycoses often poses management problems as it requires regular and long-term antifungal administration. The information concerning pharmacokinetic properties among animal species and guidance for veterinary treatment regimen is however largely unavailable due to the fact that the majority of antifungal drugs extensively used in animals are only approved for human use [12]. Often time, the treatment regimens resulting in unfavorable clinical outcomes could lead to the development of resistant strains. Moreover, some fungal diseases essentially cryptococcosis and dermatophytosis are also zoonosis [13].

3. Conventional antifungal drugs and their clinical limitations

Practically, the antifungals available in veterinary market are the same as those developed for the human markets but with modified strengths [12]. Since an increasingly important role of fungal pathogens in human diseases such as compromised immunity associated with organ transplantation and human immunodeficiency virus infection has become more prevalent during past decades, the search for the more effective and less toxic compounds for treatment of fungal diseases has been vigorous. Veterinarians have gained access to a rapidly expanding list of antifungal drugs with high efficacy and low toxicity for the treatment of mycotic infections particularly in companion animals [14]. The summary of currently available antifungals for systemic and topical treatment of animal mycotic diseases is presented in Tables 1 and 2. Nonetheless, it is noteworthy that the adverse effects among antifungals and among animal species have still been evident mostly in systemic administration. This could be a result of a general lack of applicable clinical literature for antifungal use in a given animal species, which leads to an extrapolation on the interpretation and use of MIC data. In addition, different pharmacokinetic properties of the antifungal drugs across animal species as well as in the pregnant and young animals may contribute to the observed side effects. Consequently, the veterinary practitioners and owner’s concern over possible side effects of systemic and oral drugs has increased in recent years, resulting in more favourable acceptance of topical therapy despite the greater requirement of the owner dedication, time and money [15].

4. Re-emergence of antifungal herbs as the treatment of choice

Fungi are able to improve resistance against conventional drugs rapidly, prompting the constant need to identify novel antifungal agents. Among the natural sources for therapeutic substances, plants have always played a classic role for such purposes since the dawn of human history. The application of medicinal plants has long been an integral part of both human and veterinary medicine and the practice is still rather common in Asian countries, including China, India, Japan, Pakistan, Sri Lanka and Thailand [1]. Reports from Latin and South America (Mexico, Brazil and Colombia), Europe (Finland and Italy) and Africa (Tanzania and Ethiopia) also demonstrate long-stand values of ethnobotanical remedy for treatment of mycotic diseases [2, 16-19]. The interest in antifungal activities of plants and plant-derived compounds extensively noted from around the world during the past decades is therefore a renewed concept with science-based approaches.

Thus far, it has been estimated that more than 10,000 species of plants are used medicinally and more than 100,000 plant products have been described for their pharmacologig properties [1, 19]. An exhaustive list of plants, plant extracts, and isolated plant compounds shown to exhibit antifungal activity has been developed [19, 20]. According to the recent proposed IC\text{50} < 100 \mu g/ml or MIC < 500 \mu g/ml to be a cut-off value to validate that the extracts possess any promising therapeutic value [7, 21], the potential plant candidates with antifungal effect are tabulated in Table 3. It is noted, however, that standard susceptibility testing has not been available for all tested organisms. In addition, the majority of the preclinical data has been derived from testing of the extracts against Candida spp. and, to a lesser extent, filamentous fungi. This is likely due to the comparative ease and reproducibility of yeast-based experiments, as well as a significant prevalence and economic importance of Candidiasis in humans [19, 20].

As mentioned earlier, the increased incidence of dermatophytic infection in veterinary species and the growing evidence of resistance has raised greater concern during the past decades due to its zoonotic potential, particularly between children and companion animals such as cats, dogs, birds and small rodent/pocket pets [22-24]. The adverse effects from systemic and oral application of conventional antifungal drugs have driven the owner’s favor toward topical drugs, which requires regular and long-term administration. The expense burden from continually rising prices of several conventional antifungals is therefore inevitable. In this regard, the re-emerging interest of natural products, including plant-derived antifungals, could provide a niche for herbal formulations against dermatophytosis in animals with possible better affordability.

In the Southeast Asian region, the commonly studied plants with antifungal activity include Allium sativum, Piper betle, Rhinacanthus nasutus, and Senna alata (formerly Cassia alata) (Table 4). Among the outstanding candidates with antidermatophytic activity, P. betle has been extensively investigated [8, 25, 26]. It is a tropical plant.
<table>
<thead>
<tr>
<th>Antifungals</th>
<th>Spectrum and Clinical applications</th>
<th>Adverse effects</th>
</tr>
</thead>
</table>
| **Polyenes: Amphotericin B** | - Broad spectrum.  
- Systemic treatment of filamentous fungal infections, life-threatening yeast or dimorphic fungal infections, including blastomycosis, histoplasmosis, cryptococcosis, coccidioidomycosis, candidiasis, sporotrichosis and pythiosis.  
- Treatment of systemic mycoses that fail to respond to azole therapy. | - Dose-related renal toxicity due to both vasoconstrictive and tubulotoxic effects.  
- Pyrexia, tremors, nausea, malaise and depression during intravenous administration in some animals.  
- Possible thrombophlebitis, hypokalemia, cardiac arrhythmias and non-degenerative anemia.  
- Doses higher than 5 mg/kg of conventional amphotericin B in dogs could result in death due to cardiac abnormalities. |
| **Pyrimidine synthesis inhibitors: Flucytosine** | - Effective against yeast and some *Aspergillus*.  
- Used as an adjunct to amphotericin B for cryptococcosis treatment. | - Reversible anorexia, nausea, diarrhea and vomiting.  
- Dose-related bone marrow suppression.  
- Skin eruptions characterized by depigmentation, ulceration, exudation and crust formation.  
- Seizures and abnormal behavior may occur in cats. |
| **Azole antifungals:**  
- Imidazoles: Clotrimazole and Ketoconazole  
- Triazoles: Fluconazole, Itraconazole and Voriconazole | - Broad spectrum.  
- Initial drug of choice for all but the most rapidly progressing and most severe systemic fungal infections. | - Dose-related gastrointestinal irritation.  
- Hepatotoxicity (ketocanazole).  
- Suppression of adrenal and testicular steroid synthesis as well as embryotoxic and teratogenic effects (ketocanazole).  
- Cataracts after long-term ketoconazole therapy.  
- Thrombocytopenia (ketocanazole and fluconazole).  
- Pharyngeal and upper airway irritation as well as CNS irritation and seizures (clotrimazole).  
- Dose-related local ulcerative dermatitis (itraconazole).  
- Reversible visual disturbances and dermatopathies (voriconazole). |
| **Allylamines: Terbinafine** | - Broad spectrum.  
- Hepatotoxicity (rare).  
- Neutropenia or pancytopenia (rare). |
| **Echinocandins:**  
- Caspofungin | - Treatment against candidiasis and aspergillosis. | - Fever, nausea and phlebitis at the infusion site. |
| **Griseofulvin** | - Systemic treatment of dermatophytic infection. | - Gastrointestinal irritation: diarrhea, anorexia and vomiting.  
- Bone marrow suppression.  
- Hepatotoxicity and CNS signs.  
- Teratogenic effect in cats and the use is contraindicated in pregnant animals.  
- Not to be given to kittens less than 12 weeks of age or cats with FIV positive. |

References [10, 12, 14, 30-32].
Table 2  Antifungal drugs for topical treatment.

<table>
<thead>
<tr>
<th>Antifungals</th>
<th>Spectrum and Clinical applications</th>
<th>Adverse effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polyenes: Natamycin</td>
<td>Filamentous and dimorphic fungi and yeasts.</td>
<td>Mild and locally irritating.</td>
</tr>
<tr>
<td>and Nystatin</td>
<td>Local treatment against ringworm.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cows with Candida mastitis</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Filamentous fungal keratitis and Candida metritis in horses.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Malassezia infections of the outer ear in dogs</td>
<td></td>
</tr>
<tr>
<td>Azole antifungals</td>
<td>Broad spectrum</td>
<td>Well tolerated.</td>
</tr>
<tr>
<td>▪ Imidazoles:</td>
<td>Topical treatment dermatophytes infection.</td>
<td></td>
</tr>
<tr>
<td>Miconazole,</td>
<td>Local application in mycotic keratitis and endometritis in horses.</td>
<td></td>
</tr>
<tr>
<td>Enilconazole,</td>
<td>Local treatment for yeast mastitis and mycotic endometritis in cows.</td>
<td></td>
</tr>
<tr>
<td>Clotrimazole and</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ketoconazole</td>
<td></td>
<td></td>
</tr>
<tr>
<td>▪ Triazoles:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluconazole</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Allylamines: Naftifine,</td>
<td>Treatment of dermatophytic and Malassezia infections.</td>
<td>Gastrointestinal and skin reactions, but transient and mild.</td>
</tr>
<tr>
<td>and Terbinafine</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other class:</td>
<td></td>
<td>N/A</td>
</tr>
<tr>
<td>Amorolfine,</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Butenafine, Ciclopiox,</td>
<td>Treatment of dermatophytosis.</td>
<td></td>
</tr>
<tr>
<td>Haloprogin,</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tolnaftate and</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Undecylenic acid</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

References [30, 33-36].

association with human culture can be traced back for more than 2,000 years and its role in ethnopharmacology has been recorded in many parts of the world [25-29]. Previous phytochemical and pharmacological studies have suggested that the amides and cinnamoyl derivatives found in the Piperaceae species might be responsible for their antimicrobial properties [37, 38]. Employing a direct analysis real time mass spectrometric technique, Bajpai and colleagues have additionally revealed terpenes and phenols as major constituents in betel leaves [25]. Based on the promising antidermatophytic value of P. betle extract, a 10% P. betle cream has been formulated without the addition of benzoyl peroxide [8, 39, 40]. The P. betle cream, slightly acidic and dark green in color, still maintained a characteristic odor of betel leaves. This preparation exhibited the antidermatophytic activity comparable to that of ketoconazole cream up to 96 h after incubation as shown in Table 5 [8, 41]. Moreover, the study of gel and ointment preparations containing 4% of P. betle extracts revealed a remarkable antifungal effect similar to clotrimazole cream (1%), but significantly higher than tolnaftate cream (1%). These preparations induced no rash or irritation either before or after UV irradiation in the guinea pig and rabbit toxicity tests [42, 43]. Nonetheless, due to less stability and rapid loss of activity of the P. betle preparation, further modification of the cream formulation has been suggested so that it would be more clinically applicable.

Similarly, the potent antidermatophytic effect of A. sativum extracts has been well recognized and extensively studied. Uses of the preparations of the garlic extract as 0.4% ajoene cream and 0.6% ajoene gel have been documented. Trials of these products on fungal infections of the skin, including ringworm, jock itch and athlete’s foot, yielded satisfactory outcomes comparable to terbinafine [44-46]. On the other hand, although the extracts of Rhinacanthus nasutus, and Senna alata exhibit strong antifungal activities, the formulations of their products still need much further research and development [47, 48].

5. Trends in herbal modalities and potential applications of plant-derived antifungals in veterinary medicine

The World Health Organization’s Commission on Intellectual Property and Innovation in Public Health has continuously recognized the promise and role of natural products and traditional medicines as health aid for both humans and animals, and not only in developing nations but also in developed countries [1]. The re-emerging interest in ethnopharmacological research on natural products, particularly the medicinal plants, as evidenced by numerous publications in recent decades has additionally signified the clinical potential of medicinal plants beyond traditional medical practices. It has been anticipated that the drug discovery and development may not necessarily be confined to new molecule entities, but the rationally designed, carefully standardized, synergistic traditional herbal formulations
Table 3 Plants extracts with strong antifungal activity*

<table>
<thead>
<tr>
<th>Plant</th>
<th>Main components</th>
<th>Test organism(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kaempferia galanga</td>
<td>• polyphenols</td>
<td>Saprolignea parasitica H2.</td>
</tr>
<tr>
<td></td>
<td>• flavonoids</td>
<td></td>
</tr>
<tr>
<td>Blepharispermum subsessile</td>
<td>• desmethyl isoencecalin</td>
<td>Cryptococcus neoformans</td>
</tr>
<tr>
<td></td>
<td>• 5-hydroxy-6-acetyl-2-hydroxymethyl-2-methyl chromene</td>
<td>Candida albicans</td>
</tr>
<tr>
<td>Salvia texana</td>
<td>• flavonones</td>
<td>Aspergillus fumigatus</td>
</tr>
<tr>
<td></td>
<td>• diterpenes</td>
<td>Histoplasma capsulatum</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Coccioidioes immitis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Candida albicans</td>
</tr>
<tr>
<td>Nigella sativa</td>
<td>• terpenes</td>
<td>dermatophyte fungi</td>
</tr>
<tr>
<td>Pinellia ternata</td>
<td>• pinellloside</td>
<td>Aspergillus niger</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Candida albicans</td>
</tr>
<tr>
<td>Piper regnellii</td>
<td>• phenylpropanoids</td>
<td>dermatophyte fungi</td>
</tr>
<tr>
<td></td>
<td>• neolignans</td>
<td></td>
</tr>
<tr>
<td>Inula viscosa</td>
<td>• sesquiterpene - tayunin</td>
<td>dermatophyte fungi</td>
</tr>
<tr>
<td>Elaeodendron schlechteranum</td>
<td>• triterpenoids</td>
<td>Candida albicans</td>
</tr>
<tr>
<td></td>
<td>• sterols</td>
<td></td>
</tr>
<tr>
<td>Acacia tortilis</td>
<td>• terpenes</td>
<td>Candida albicans</td>
</tr>
<tr>
<td></td>
<td>• flavonoids</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• cyclitols</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• essential oils</td>
<td></td>
</tr>
<tr>
<td>Balanites aegyptiaca</td>
<td>• unsaturated fatty acids</td>
<td>Candida albicans</td>
</tr>
<tr>
<td></td>
<td>• sterols</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• alkaloids</td>
<td></td>
</tr>
<tr>
<td>Ajania fruticulosa</td>
<td>• guianolides</td>
<td>Candida albicans</td>
</tr>
<tr>
<td></td>
<td>• sesquiterpenes</td>
<td></td>
</tr>
<tr>
<td>Xanthosoma sagittifolium</td>
<td>• polyphenols</td>
<td>dermatophyte fungi</td>
</tr>
<tr>
<td></td>
<td>• flavonoids</td>
<td></td>
</tr>
<tr>
<td>Schinus molle</td>
<td>• monoterpenes</td>
<td>Candida albicans</td>
</tr>
<tr>
<td></td>
<td>• sesquiterpenes</td>
<td></td>
</tr>
<tr>
<td>Anacardium occidentale</td>
<td>• phenolic lipids</td>
<td>Cryptococcus neoformans</td>
</tr>
<tr>
<td></td>
<td>• flavonoids</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• tannins</td>
<td></td>
</tr>
<tr>
<td>Curtisia dentata</td>
<td>• triterpenoids</td>
<td>Cryptococcus neoformans</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Sporothrix schenckii</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Aspergillus fumigatus</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Microsporum canis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Candida albicans</td>
</tr>
<tr>
<td>Inula racemosa</td>
<td>• sesquiterpenes</td>
<td>Aspergillus flavus</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Aspergillus niger</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Geotrichium candidum</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Candida tropicalis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Candida albicans</td>
</tr>
<tr>
<td>Melaleuca alternifolia</td>
<td>• terpenes</td>
<td>Aspergillus spp.</td>
</tr>
<tr>
<td></td>
<td>• sesquiterpenes</td>
<td>dermatophyte fungi</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Candida albicans</td>
</tr>
<tr>
<td>Polygonum acuminatum</td>
<td>• sesquiterpenes</td>
<td>Cryptococcus neoformans</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Aspergillus spp.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>dermatophyte fungi</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Candida albicans</td>
</tr>
<tr>
<td>Toddalia asiatica</td>
<td>• flindersine</td>
<td>dermatophyte fungi</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Candida albicans</td>
</tr>
<tr>
<td>Alpinia conchigera</td>
<td>• phenylpropanoids</td>
<td>dermatophyte fungi</td>
</tr>
<tr>
<td></td>
<td>• diarylheptanoids</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• flavonoids</td>
<td></td>
</tr>
<tr>
<td>Daucus carota</td>
<td>• sesquiterpenes</td>
<td>Cryptococcus neoformans</td>
</tr>
<tr>
<td></td>
<td>• phenylpropanoids</td>
<td>dermatophyte fungi</td>
</tr>
<tr>
<td></td>
<td>• eugenol</td>
<td></td>
</tr>
</tbody>
</table>

*IC_{50} < 100 µg/ml or MIC < 500 µg/ml [7, 21].
References [52-80].
Table 4  Plant species cited for antidermatphytic remedy in the South East Asian region.

<table>
<thead>
<tr>
<th>Botanical taxon (Botanical family)</th>
<th>Preparation</th>
<th>Active constituents</th>
<th>MIC</th>
</tr>
</thead>
</table>
| *Allium sativum* L. (*Alliaceae*) | Ethanolic or water extracts of bulbs | • allicin  
• allyl sulfide  
• allyl disulfide  
• ajoene | 1.5-6.3 μg/ml |
| *Piper betle* L. (*Piperaceae*) | Ethanolic extracts of leaves | • amides  
• cinnamoyl derivatives  
• terpenes  
• phenols | 230.0 μg/ml |
| *Rhinacanthus nasutus* L. (*Acanthaceae*) | Ethanolic or chloroform extracts of leaves and root | • rhinacanthin- A, B, C, D, and N  
• oxymethylantraquinone | 26.5-106 μg/ml |
| *Senna alata* (Fabaceae) | Ethanolic or water extracts of leaves and bark | • rhein  
• emodin, aloe- emodin  
• 4,5-dihydroxy-1-hydroxymethylanthrone  
• chrysophanol | 125 μg/ml |

References [8, 25-29, 37, 38, 81-87].

Table 5  In vitro antidermatphytic activity of 10% *P. betle* cream and ketoconazole cream.

<table>
<thead>
<tr>
<th>Compound</th>
<th>M. canis</th>
<th>T. mentagrophyte</th>
</tr>
</thead>
<tbody>
<tr>
<td>10% <em>P. betle</em> cream</td>
<td>Inhibition zone: 28.00 ± 0.12 mm</td>
<td>Inhibition zone: 32.00 ± 0.15 mm</td>
</tr>
<tr>
<td>Ketoconazole cream</td>
<td>Inhibition zone: 29.30 ± 0.03 mm</td>
<td>Inhibition zone: 35.70 ± 0.23 mm</td>
</tr>
</tbody>
</table>

Modified from [41].

and botanical drug products with robust scientific evidence can also be the attractive options [3, 49]. In addition, the global market of botanical and plant-derived compounds is expected to increase from 19.5$ billion in 2008 to 32.9$ billion in 2013 [50]. Although the recently observed upward trend in herbal and other alternative medical modalities in human health relies in part on the social, economic and philosophical reasons, the rationales underlying the similar trend in veterinary practice have not been extensively investigated. Nonetheless, it is undeniable that the accumulated scientific data supporting pharmacologic activity of plants and plant extracts have provided medical professionals the better knowledge, so that the application of plant-derived compounds and herbal formulation can be employed with a more specific purpose, better efficacy, and reduced risk of toxicity [4, 9].

In veterinary practice, the market for animal antifungals is estimated to reach $110.7 million by 2012 [51]. The treatment regimens for animal mycoses, especially dermatophytosis, with currently available antifungals resulting in
favorable clinical outcomes do not come in a “one size fits all” and oftentimes it depends rather on how much drug to use and for how long in a given animal species, not the choice of drug [11, 14, 15, 30]. The growing favor towards the topical antifungal therapy undoubtedly further enhances the need for longer-term drug administration, i.e. several months, in most cases. As a consequence, some ingredients such as benzoyl peroxide usually found in conventional formulations could create more risks of observable adverse effects in the patients [39, 40]. The attempts in developing the antifungal herbal formulation for topical uses would then provide the possible safer treatment of choice, but also generate the niche in the animal antifungal market and a more affordable animal health aid [8, 41, 44-46]. The hair coat of animals, however, can limit the use of creams, gels and ointments, particularly when animals try to remove topical agents by licking. Formulation as shampoos and moisturizers to be used as sole therapy to resolve clinical signs or as an adjunct and applied at the right dosing schedule could also be effective [11, 14, 15, 30].

Despite the vast potential and possibilities associated with plant products with antifungal properties, drawbacks in application remain, particularly in compound stability and bioavailability. Seeking strategies to prolong the product shelf-life as well as searching for new synergistic combinations in order to improve bioavailability would be of interest and could play a significant role in drug development. Such stability and bioavailability enhancing activity may have numerous advantages in drug development including reduction in dose, toxicity and treatment costs [3, 49].

6. Conclusion

As it becomes necessary to identify and develop novel antifungal compounds and the shift in favor of topical application particularly in dermatophytosis treatment in companion animals, the potential role of plants/ plant extracts as sources for new antymycotics has never been more apparent. The recent and renewed interest in medicinal plants inspired by traditional wisdom and the development in information technology have facilitated an explosion in the range and content of electronic information concerning antifungal medicinal plants and herbal formulations as a re-emergent treatment of choice with comparable efficacy, but perhaps safer and more affordable. Despite the great opportunity for research and development of herbal formulation with antifungal effect, the long path between the robust scientific approval of such activity and the entree of a drug onto the market still exists.

Acknowledgements  The author expresses her gratitude to the Ministry of University Affairs of the Royal Thai Government for research grant. Dr. James A. Will of University of Wisconsin-Madison, School of Veterinary Medicine is acknowledged for his kind help in proved reading this manuscript.

References


©FORMATEX 2011


