External application of essential oils in animals.

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I. Phytotherapeutical use of essential oils in veterinary medicine

Evidence-based veterinary phytotherapy is still in its infancy. Especially the phytotherapeutical use of essential oils in animals is mainly based on anecdotal reports and experiences of veterinarians, aroma therapists and pet owners. The complaints which are commonly treated with essential oils, for example, in horses, poultries, pigs, dogs, cats and rabbits, concern the digestion system, skin infections, wounds, inflammations, respiratory ailments and diarrhoea. Essential oils enter the body in three ways: (1) applied to skin; (2) inhaled or (3) ingested. For external application, it is generally recommended to use essential oils in concentrations of 3 to 5% diluted in carrier oil, such as sweet almond oil, apricot kernel oil, jojoba oil, avocado oil, and olive oil, or embedded in creams, liniments, sprays, tinctures, and shampoos.

(a) For example, lavender oil (*Lavandula angustifolia*) can be used on the skin for cuts and minor burns, and it can also be inhaled to promote relaxation and sleep.

(b) Essential oils can also be massaged locally to alleviate pain. For that reason, some drops (approximately 30-50µl) of essential oils, such as juniper oil or rosemary oil, dissolved in carrier oil can be applied to skin area with gentle rubbing.

(c) A blend to control pet odor may consist of lavender oil, geranium oil and lemon oil. It is recommended to add one or two drops of the essential oil mixture to carrier oil, and subsequently massaged gently for 3 to 4 minutes into hairless or least hairy area of the skin, such as armpit, groin or thigh.

(d) To calm down nervous or hyperactive dogs, it is reported to place a few drops of lavender oil on the dog´s bed or sleeping area or rub a little on the food pads.

(e) Fleas hide within the pet´s fur as well as in carpets, parquets and window coverings. A blend for the treatment of flea infested animals is claimed by an USA patent. In this case a mixture of pennyroyal oil, eucalyptus oil, cedar oil, citronella oil and rue oil inserted into apricot kernel oil, olive oil or almond oil up to a concentration of 7% is recommended.

(f) To combat ticks, a mixture of TTO (10 drops) and lavender oil (10 drops) dissolved in carrier oil (all together 10 ml) is recommended. In this context, the question poses if essential oils are able to affect ticks. In an *in vitro* experiment the acaricidal effect of TTO against nymphs of *Ixodes ricinus* (tick) was examined. It could be shown that 8 to 10 µl TTO was lethal for more than 80% of the ticks when TTO was inhaled. The effect correlated very well with the duration of exposure of ticks to TTO, with a significant effect after 90 minutes of exposure. This finding shows that TTO seems to be useful in controlling ticks on dogs because ticks are efficient vectors of pathogens.

(g) Essential oils are also widely used for parasitic mite infection control in honeybee colonies. Laboratory and field tests have shown that essential oils are very effective (50 to 95%) against *Varroa destructor* and *Acarapis woodi*. *Varroa destructor* is an ectoparasite whereas *Acarapis woodi* lives in the tracheal tubes of honeybees. The volatile oils are used in bee hives either as fumigants, or mixed with sugar syrup for ingestion by bees. The last finding is that microencapsulated menthol is a new formulation which can be added to honeybee feed for an effective mite infection control.

II. Antifungal effect of TTO on *Malassezia pachydermatis* isolated from canines suffering from cutaneous disease

While human skin is usually colonized by lipid-dependent *Malassezia furfur*, from the skin of wild and domestic carnivores, such as dogs, cats, bears, ferrets and foxes, *Malassezia pachydermatis* can be recovered. The yeast exhibited a short oval to ellipsoidal cell shape and a typical unipolar budding reproduction procedure (**power point image 9**). Particular in dogs and cats *Malassezia pachydermatis* plays an important role in the pathogenesis of otitis externa and seborrhoic dermatitis. Additionally, a high colonization rate of the yeast was found on parts of the body with poor air circulation, for instance, in interdigital areas (**power point immage 10**) as well as of the anus, rectum, anal sac and vagina. Besides *Mallassezia pachydermatis* a concurrent colonization by coagulase-positive staphylococci such as *Staphylococcus aureus* and *Staphylococcus intermedius* has been frequently demonstrated. The diagnosis of these infected skin lesions was characterized by pain, unrest, pruritus, erythema and a local loss of hair.

In clinical practice miconazole or ketoconazole shampoos combined with chlorhexedine or selenium sulfide shampoos have been commonly used. In order to look for an alternative agent we determined the minimum fungicidal concentration (MFC) of TTO against five

clinical strains of *Malassezia pachydermatis* in comparison to terbinafine-HCL (**power point immage 11**).

TTO inhibited all test strains at uniform low concentrations of 560 to 1120 µg/ml. As expected the susceptibility of the tested yeasts to terbinafine-HCL was prominent with MFC values of 0.4 to 1.6 µg/ml.

In addition, apart from its antimycotic effect, TTO displayed also a remarkable antibacterial activity against different staphylococci species with MIC-values of 1200µg/ml to 5000µg/ml (**power point immage 12**). This finding means that two microorganisms both involved in acute and chronic dermatitis can be inhibited at the same time by TTO *in vitro*. Therefore, clinical trials are needed to proof its efficacy in vivo.

III. Topical use of a 10% TTO-containing cream against canine localised pruritic dermatitis

The prevalence of dermatological disorders in animals has been shown to be more than 10% of all consultations in veterinary practices. Standard therapies for canine dermatitis include antiparasitics, antibiotics, antimycotics and glucocorticoids, administered both topically and systematically. Glucocorticoids and antibiotics are frequently misused pharmaceutical substances, responsible for well-known subsequent clinical adverse reactions. As a possible alternative treatment, we tested a standardised 10% tea trea oil cream against a commercial skin care cream (with hydroxybenzoat) in the management of canine localised acute and chronic dermatitis.

Fifty-seven dogs with clinical manifestations of mostly pruritic skin lesions or alterations, corroberated by predominantly positive fungal and bacterial skin isolates, were enrolled by seven practising veterinarians. The study was perfomed as a randomised, controlled double-blind, multi-centre clinical trial. The dogs were randomly allocated to two study groups: 28 in the TTO group (10% TTO cream) and 29 in the control group (commercial skin cream). Blinding was conducted by filling the two different creams in identical white tubes. The pet owner was instructed how to apply the cream by another person, otherwise not involved in the study. The test creams were administered twice daily (dose: 25 mg of the 10% TTO cream per cm^2 of skin was applied).

Overall efficacy of treatment: After 10 days of treatment (**power point immage 13**) the overall efficacy was scored at 71% as very good or good in the TTO group, whereas only

41% of the dogs in the control group had this score. The results of the two study groups differed significantly (p=0.04).

Assessment of pruritus, erythema and alopecia: Efficacy results relating to individual improvement of the three most frequently occuring clinical signs in the study, pruritus, erythema and alopecia (**power point immage 14**), were also analyzed on day 10 and compared to day 0. Differences between the two study groups, due to clinical sign "severity changes" from resolved to improved to unchanged or to worse, were significant for pruritus (resolved: 24 dogs at day 0 to 12 dogs at day 10) and alopecia (resolved: 20 dogs at day 0 to 15 dogs at day 10), both in favour of TTO cream.

In summary, ten days after beginning the study, clinically relevant and statistically significant improvements in favour of the 10% TTO cream were seen after symptomatic treatment of localised pruritic dermatitis manifestation. The control cream, a commercial skin care cream preserved with hydroxybenzoat (antiseptic chemical), also turned out to be efficacious after 20 days, probably demonstrating a slower self healing process combined with antiseptic effects. The positive clinical effect of the 10% TTO cream is assumed to depend on previously documented antibacterial, antifungal and the demonstrated antiprurigenous effects of its active plant-based component TTO.

IV. Species specific differences and toxicological aspects

When using essential oils, veterinarians and aroma therapists must consider the differences between species and between herbivores and carnivors, along with other factors, like size and sex. ***For example***:

1. Dogs can utilize carotinoids from plants to synthesize retinol, but cats require preformed Vitamin A from animal tissue.
2. Dogs can use either fish or plant sources of omega-3-fatty acids, whereas cats require fish because they lack in delta-6-desaturase. Cats can synthesize neither eicosapentaenoic acid from α-linolenic acid nor arachidonic acid from linoleic acid.
3. Essential oils are rapidly absorbed orally and dermally. Terpenes are metabolized by the liver to glucuronide, glycine and sulfate conjugates. Repeated exposure can cause induction of the hepatic cytochrome P-450 and uridine diphosphate-glucuronyl transferase enzyme systems. Glucuronidation is an important detoxification mechanism present in most animals except in cats. Cats are therefore highly sensitive to essential oils as their liver is lacking in glucuronyl transferase activity. Lack in this

enzyme system may result in slower elimination of terpenes and thus build up of toxic metabolites in the body of cats causing toxicity problems.

4. On the other hand, essential oils are not associated with a higher incidence of adverse side-effects or intoxications than from ingestion of prescription or OTC pharmaceuticals. In most cases of reported adverse side effects, essential oils were used to treat dermatological conditions at inappropriate high doses. For instance, a dog was exposed to 2 g of pennyroyal oil per kg body weight due to its flea repellent activity. Histopathological examination of liver tissue showed massive hepatocellular necrosis. The toxin in pennyroyal is thought to be pulegone which is bioactivated to a hepatotoxic metabolite called menthofuran. It is clear that in this special case pennyroyal oil was extremely overdosed.
5. The most common clinical signs after dermal exposure of inappropriate high concentrations of essential oils include ataxia, muscle weakness, depression, and behavioral abnormalities. For instance, transient paresis was seen in small-breed dogs when TTO was applied down the spine as a topical flea treatment. Cats have developed scrotal dermatitis after exposure to D-limonene or linalool.

V. Conclusion

1. Evidence-based veterinary phytotherapy is still in its infancy.
2. At present, the use of essential oils in animals is exclusively based on anecdotal reports and experiences of aroma therapists and pet owners.
3. So called aroma therapists are mostly laymen and subsequently lacking in a medicinal background.
4. Our first clinical trial with TTO in dogs have shown that an evidence-based use of essential oil in animals is possible.
5. When using essential oils in animals species specific differences have to be taken in account.
6. Essential oils are powerful biological agents which should be used in appropriate doses, indicated ailments, during a limited time period and with care.