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SMALL MAMMALS BEE VENOM TREATMENT FOR ONCOLOGY PATIENTS

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Abstract:
The overuse and misuse of antibiotics has been linked to the emergence and spread of resistant microorganisms resulting in ineffective antibiotic treatments and posing a serious risk to public health. Bees produce many products like honey, propolis, royal jelly, bee pollen, beeswax, and bee venom, that contain bioactive constituents which have been used by many different civilizations for centuries to treat a variety of illnesses.[1] Apitherapy refers to the use of these bee products for treating health disorders and this science has been practiced for thousands of years in Asia, Africa, and Europe. In the English literature, Dr Bodog F. Beck used the term “Apitherapy” for the first time in 1935. He recommended the use of this word to describe the therapeutic use of bee products, while also acknowledging that the word is a heterogenous mix of Latin and Greek, and the more correct term would be ”Melissotherapy”.[2]

Apitherapy's roots trace back to ancient civilizations where honey and other bee products were used for wound healing, treating respiratory issues, and treatment other ailments. Modern peer-reviewed apitherapy studies in human medicine suggest that these substances have anti-inflammatory, antimicrobial and even anti-neoplastic properties [2-4].

While there is much scientific evidence available regarding the efficacy of apitherapy, it still is not accepted by many practitioners of Western medicine. There are multiple reasons for this dichotomy and some of them include the following: A lack of standardization of the products themselves does not allow for broad clinical trials, and trials that are attempted often do not yield repeatable results. This lack of standardization in the products also means that large-scale production is often not possible, which in turn hampers profit-making and leads to variabilities in product specifications regarding its shelf life, active ingredients, etc.

Also, most apitherapy products consist of an amalgamation of multiple biologically active substances which act in synergy to achieve results. Very often the mode of action is not well understood. For example, bee venom consists of a multitude of proteins, each of which might contribute to any given therapeutic effect, much like an orchestra where many different instruments are playing together to create the final musical experience. As an example of this oversimplification, Mellitin is the major protein in bee venom, making up about 50% of the dry matter substance. Frequently medical studies on the effects of bee venom have used only this single protein when attempting to explain the effect of what a mix of many different proteins is essentially. Therefore, conclusions of effects are understandably difficult to make.
The author accepts the lack of scientific explanations of these mechanisms and has focused on the *in vitro* and *in vivo* studies which document a clear anti-neoplastic activity even without necessarily being able to explain the exact mechanism of action. Without a doubt there is a significant amount of evidence in the peer-reviewed literature showing the efficacy of apitherapy products regarding their anti-neoplastic efficacy on cancer cells, and this fact should not be ignored.
Another factor which might cause skepticism regarding apitherapy is the fact that observations and publications are often anecdotal, and case based and not based on clinical trials. These publications are also frequently published outside the USA in countries where apitherapy is more widely accepted. The scientific rigor of these publications is often questioned as knowledge of standards of publications and research are not well known to the readers in the USA.
Another issue with the acceptance of apitherapy is the lack of standardization of the products themselves. In contrast to industrially manufactured drugs, the products produced by bees exhibit a seasonal and

geographical variation which might impact their efficacy. This variation makes reproducibility of effect between products from different geographic regions more difficult. Because of this variation, especially in products that are dependent on the floral environment, publications which highlight their effects on cells *in vitro* or *in vivo* usually contain the geographic details regarding the origin of the product (e.g. green propolis from Brazil)

A reason for the large number of publications being from outside the USA could be that integration of alternate therapies is more frequently seen as an option in health care in other countries. For example, in Brazil apitherapy tends to be an expanding practice and has become part of the National Policy of Integrative and Complementary Practices (PNPIC – Ministry of Health, Regulation 702, March 21, 2018).[3] Cultural and philosophical aspects of society can also be a factor in promoting a more holistic approach to healthcare when compared to the USA.
The legal landscape in the USA for using apitherapy in exotic species involves navigating the veterinary laws concerning possession, treatment, and ethics. As new problems develop, new legislation may be created, impacting how such treatments can be applied. Practitioners must stay updated with these laws to ensure compliance and to minimize the risk of liability.
One legal resource that might be useful to the practitioner is the “Right to Try Act” from the Food and Drug Administration (FDA) especially for an oncological case where traditional treatment is not feasible. The “Right to Try Act” is one way for patients who have been diagnosed with life-threatening diseases or conditions, who have tried all approved treatment options, and who are unable to participate in a clinical trial, to access certain investigational treatment options. FDA’s role in implementing the “Right to Try Act” is limited to receiving and posting certain information submitted to the agency (see https://tinyurl.com/FDARTT).

Economic factors are often yet another factor and promotes apitherapy in populations which cannot afford more expensive pharmaceuticals.

A comprehensive review of the evidence for the medicinal use of natural honey in animals was recently published and highlights many of the details discussed in this lecture. [4] The bottom line is that scientific evidence exists that apitherapy has a multitude of beneficial effects which vary depending on the product being used. Some of the well documented benefits include antibacterial, anti-inflammatory, anti-mutagenic, anti-proliferative properties, anti-oxidant, anti-parasitic, antitumor, cardiovascular protector and healing. [5-8]

While the field of apitherapy still needs a great deal of research, it is clear that there are important therapeutic gains to be made through the use of these products. One of their benefits may lie in their use as adjuvant therapies in combination with other well documented pharmaceuticals.

In the author’s opinion there is currently ample evidence in the literature demonstrating the use of apitherapy products *in vivo* and *in vitro* to justify the use of these products in an affected patient. For example, in human medicine apitherapy using bee venom is gaining momentum and forms are available online to document informed consent. Online resources on the use of apitherapy in the veterinary field exist which can also provide guidance and be a resource for the inquiring practitioner. The author recommends the American Apitherapy Society as one of these resources (see https://apitherapy.org/en).

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