

Review

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Posted Date: 5 October 2023

doi: 10.20944/preprints202310.0265.v1

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Review

Action of Viscus Album L. on Diabetes and Hypertension in the Veterinary Field

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Abstract: Viscum album L., also known as “Mistletoe”, is a hemiparasitic plant native to the European continent that grows on various host trees. This plant contains a wide variety of active compounds that can be used to treat various diseases, such as diabetes, hypertension, as an anti-inflammatory and antioxidant. However, it is most indicated in human medicine for the adjuvant treatment of cancer patients. Both for its properties directed against neoplastic cells and for its antioxidant and anti-inflammatory properties. In Veterinary Medicine, very few studies are recorded for animals, although formulations are available for commercial use in oral and injectable form, mostly for homeopathic use. Many studies have been conducted on a large scale by groups of independent researchers and doctors in several countries, such as Switzerland, Germany and Brazil. Therefore, this review aimed to collect data on the use of Viscum album in Veterinary Medicine in order to encourage research in this sector not only in oncological diseases but in other directions in which Viscum can find use as an anti-hypertensive and anti-diabetic agent. Introduction: Lectins, flavonoids, phenols such as phenylpropanoids, coumarins, sterols, lignans, terpenoids, phenylpropanoids, alkaloids, fatty acids and viscotoxins are among the main active ingredients present in the phytocomplexes of the Viscum album plant. In particular, Attention should be given to specific oligoproteins in consideration of their biological activity [1]. present in The foliage and fruits of V. album, as in other related species, contain low-weight proteins molecular type of thionin, called viscotoxins, as well as characteristic lectins, called viscolectins, both can contribute to its system defense and can be found in extracts and related products. These classes of Viscum microproteins have received considerable attention due to their contribution to cytotoxic and immunostimulant effects of mistletoe extracts used in medicine, as discussed later, including their mechanism of action [2,3] viscotoxins can increase the number of cells circulating natural killers and consequently improve the response host antitumor immunity [8]. Likewise, the viscotoxin has an effective immunomodulatory impact on human and animal granulocytes [9,10] and also acts on cellular apoptosis [11]. The cytotoxic action of viscotoxin is comparable to that of conventional chemotherapeutic agents [12].

Keywords: Viscum album; Paolo Pelini; veterinary medicine; hypertension, diabetes

Literature survey

In the 20th century, excerpts from the Viscum album were cited by Rudolf Steiner (1861-1925) and Ita Wegmann (1876-1943) around 1917 with the emergence of anthroposophic medicine and were linked to the treatment of cancer patients. The first publication on this topic is dated 1933 [5]. Steiner and Wegmann recommended that the active ingredient Viscum album should be extracted from the plant in two seasons of the year where the balsamic weather is maximum (summer and winter) to obtain therapeutic activity more effectively [6], considering the defense system of plant and the synthesis of various substances during the seasons [7]. Reports on the use of Viscum album therapy in Veterinary Medicine began to be systematically identified starting from 1979, when Petkov began using these extracts intravenously and obtained satisfactory results in the control of blood pressure in dogs [13]. Throughout history, therapy with Viscum album has been successfully administered to cancer patients in various species [14,15]. Furthermore, Bowman confirmed the hypotensive activity

of the *Viscum album* extracts administered intravenously to dogs e he underlined the beneficial cardiovascular effects on these animals. Among the various properties of the *Viscum album* plant, those stand out antitumor, cardiostimulant, antidiabetic, hepatoprotective, antioxidant, antibacterial, antifungal and immunomodulatory. The latter has been described in humans since the beginning of the 19th century.

In animals, the immunomodulatory activity of *Viscum* extract album was recorded when it was applied on the street subcutaneously and intravenously in rabbits, influencing the parameters immunological in an "in vivo" experiment. This medicine has significantly increased the synthesis of lymphocytes, in particular the natural killer and phagocytic activity of granulocytes.

The hypoglycemic properties of *Viscum album* extracts are were described by Ohiri et al. [16]. The study reported control of glycemia in diabetic animals induced by alloxan. The experiment involved the administration of doses of 200 mg/kg and 400 mg/kg of body weight that significantly reduced blood sugar blood in fasted normal albino rats and rabbits, respectively alloxanized. Fasting blood sugar, measured in n milligrams per 100 ml, was reduced by 30.06% in normoglycemic rats, while in alloxanized rabbits, blood glucose was reduced from the mean value of 650 ± 7.2 mg% at zero hours to 87 ± 8.2 mg% at 4 hours. The effects of glucose-lowering drugs were compared with those of tolbutamide. Acute toxicity studies of the extract in mice showed an LD50 value of 4.18 ± 0.96 g/kg body weight when administered intravenously.

Furthermore, Turkkan et al. [17] have demonstrated the activity of extracts of *Viscum album* in a conventional experimental rat model with streptozotocin (STZ)-induced diabetes to evaluate the effects of this medicine on lipid peroxidation and system antioxidant. The experiment was performed with 32 divided adult rats in four groups of eight rats each: Group – control (STZ); Group 2 - test 1 (VA); Group 3 - test 2 (VA + STZ). The extract of the *Viscum album* was administered orally for ten days. Fasting blood glucose level was measured and recorded. The animals were sacrificed and catalase was measured (CAT), malondialdehyde (MDA) and proteins present in the samples of liver and kidney tissue. After statistical analysis, it was discovered that oxidative stress was associated with diabetic complications. *Viscum album* extracts given to diabetic rats reduced oxidative stress and improved their overall condition. However, despite the promising results obtained in this work, the authors stated that more are needed studies to increase understanding of the potential antidiabetic and antioxidant effects of *Viscum album* therapy.

Bello et al. [18] studied the antidiabetic activity of the extract aqueous of *Viscum album* leaves, in vivo, and compared the its antidiabetic efficacy with that of the drug metformin. Biochemical analysis demonstrated a significant dose reduction dependent ($P < 0.05$) on serum glucose levels in treated rats with *Viscum album* leaf extract. This result was observed when groups treated with *Viscum* albums were compared with diabetic and metformin-treated control groups. Likewise, there was a significant decrease in total cholesterol, triglyceride and low-density lipoprotein levels which were elevated before treatment with the leaf extract. AND a correspondingly significant increase was observed high-density lipoprotein levels compared to the control group diabetic. The plant extract significantly reduced ($P < 0.05$) the serum activities of marker enzymes: alanine and aspartate aminotransferase. Similarly, a significant reduction ($P < 0.05$) in creatinine and urea levels was detected in the groups treated with *Viscum album* extract and metformin compared to diabetic control group. Furthermore, the plant extract attenuated the weight loss recorded in the diabetic control group. The aqueous extract of *Viscum album* leaves has demonstrated high antidiabetic activity, comparable to that of metformin.

Year	Author	Species	Purpose Treatment	Administration route
1979	Petkov	dog	Antihypertensive	Intravenous
1989	Hajto et al	Rodent	Immunomodulation	Subcutaneous/ Intravenous
1990	Arciere	dog	Antihypertensive	Intravenous
2003	Ohiri et al	Rodent	Hypoglycemic	Intraperitoneal
2019	Bello et al	Rodent	Hypoglycemic	Oral

Conclusions

According to the data presented in this review, the *Viscum album* is a potential to aid in the treatment or as an adjunct for these pathologies in animals. Further studies are needed on the real potential of *Viscum album*, its impact on the quality of life of treated animals, mechanisms of action, metabolism, among others.

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