Application possibilities of Humic Acids in Veterinary

1. Structure and toxicity

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Introduction:

The diseases of the digestive system can be divided into different groups (enteritis, diarrhoea, dyspepsia). The therapy of these diseases is getting harder and harder because more and more active ingredients are getting into the animals from the antibiotic and chemotherapy products. Because of these facts unfavourable side effects can be expected like resistance, toxicolgical side effects, allergy and immune system problems. All these problems emphasise the importance of prevention and application of alternative methods. The directives of the EU also show strict regulations regarding the application of antibiotics.

In case of the new active ingredients the important question is not only how effective they are as antibacterial and antiviral products but at least so important that they should not have harmful side effects. The most important requirement of these alternative ingredients that they should not be toxic (not even their metabolits) should not cause harmful immune and allergic reactions and furthermore should be effective against the given disease mainly in the prophylaxis but also in the therapy.

In this study I would like to prove that humic acids fulfil all these requirements and may open a new chapter in veterinary and feeding as alternatives of some antibiotics and chemotherapy products or briefly as economical products to improve the feed utilization.

Formation and classification of Humic Acids

Humic Substances are forming during the so called humification and coal formation processes of the plant biomass (plant, peat, lignite, brown coal, black coal, antracite, graphite). Humic acids start to from in the peat phase but they decompose still in the black brown phase. Humic acids being natural polymer molecules form a wide molecule size spectrum, the transition is continous between the groups. According to the International Humic Substance Society humic substances can be divided into the following groups:

Humic acid (singular): the biggest molecular size group (M= 1000-5000) soluble in alkalic but insoluble in acidic solutions.

Hymatomelanic acid: medium molecule size group (M=600-900) soluble in alkalic and alcoholic solutions but insoluble in acidic.

Fulvic acid: the smallest size group (M= 300-600) soluble in alkalic and also in acidic solutions.

Humic acids (plural): collecting name for the humic acid, hymatomelanic acid and fulvic acid

Humates: salts of humic acid (Fe-humate)

Structure of humic acids

Humic acids are 3 dimensional macromolecules natural polymers building from similar structure monomers. They consist of a quinon structure central unit which contains hydroxil and carboxyl groups. Depending on the raw material from which the humic acids are extracted and also on the technology of the extraction in the literature several other molecular groups are mentioned as humic substances (carbohydrate like molecules, flavonoids and lignin derivatives etc.) (3,4,9)

The structure analysis of humic substances proved that the most important functional groups are the quinon, aromatic carboxyl and hydroxyl (3,5,9). These groups are able to form complicated 3 dimensional structures, depending on the pureness and origin of the samples. In natural form these functional groups may bond to several inorganic (Ca, Mg, Fe etc,) and organic decomposition residues (carbohydrates, plant waxes, proteins, lignins, flavonoids etc,). It must be emphasised that the presence of these non humic residues cause several misunderstanding in the literature and in the practice as well.

Humic acids may be considered as natural quinon compounds because their basic aromatic quinon structure is able to take part in biochemical reactions as electron donor and acceptor molecules. I call humic acids as biologically active molecules because of this ability.

The main chemical and biochemical reactions of humic acids are based on the following 3 characteristics:

Forming complexes: The aromatic hydroxil and carboxyl groups form metastable complexes with metals and other cations. The bigger the molecular weight of the metals the stronger is the complex. This ability means that humic acids help the uptake of the useful micronutrients (lower molecular weight) while remove the toxic metals (heavy metals) from the organisms acting as detoxicant.

Biological activity: Thank to the quinon groups humic acids are able to take part in the energy production reactions of the cells as electron transfer catalyst (cell respiration catalyst). These reactions are similar to the effects of the redox coenzymes (ubiquinon, FADH, NAD) (2,4). Partly this ability is the reason of the immune system stimulating and roborant effets of humic acids. Regarding the biological activity there is

an other important effect that is a strong reducing effect which is almost as strong as that of the vitamin C. Humic acids give all the characteristic reactions of ascorbic acid. This reducing effect play an important role in the biochemical reactions of iron. (1.)

Physicochemical adsorption: The large specific surface and the micella structure gives an effective adsorption better than the active carbon. This is the reason of the realised good anti diarrhoea and detoxication effects.

The antiviral and antibacterial effects of humic acids are the results of complex processes that will be mentioned in the next part.

Toxicological study of humic acids

During the prophylactic and therapeutic application of humic acids the most important condition is that they should not cause any toxic side effects and genetic modifications. Below we make a short summary of the toxicology studies made by us or found in the literature. (6,7).

Oral ip. and iv. applications

The experiments were carried out mainly by Na-humate and humic acid preparations. The results are summarised in the TABLE 1. (7).

***TABLE 1**. LD_{50} values of Na-humate*

Animal	Application	**LD_{50} mg/kg**
Rat	*oral*	*11500*
Rat	*i.p.*	*200*
Rat	*i.v.*	*55*
Mouse	*i.v.*	*90*

Humic acids are applied mainly as oral products in the dose range of 200-1000 mg/body-weight-kg. From the oral LD_{50} value it is obvious that humic acids are practically non-toxic molecules and they cannot be overdosed. During the tests on mice, rats, rabbits and guinea-pigs the parenteral and peroral overdose of an 1 % humic acid solution did not cause any toxic effects. Moreover the intravenous application of the 10 ml/body-weight-kg dose proved to be harmless (1.).

Praenatal studies

The praenatal studies play an important role to find out the toxicological behaviour of humic acids during several generations and also to consider the embryotoxic and teratogene effects.

From the results of these studies we can conclude that during the oral and intra-parenteral applications toxic side effects cannot be expected.

The experiments did not show any deformation in the formation of bones. There were not any signs of macroscopic or microscopic degeneration or abnormal cell proliferation or retard development (6,7.)

TABLE 2.

TABLE 2. Praenatal toxicologycal study of Na-humate on rats (10 pcs of mother animals)

Dose mg/kg	**Implantation/ mother**	**Number of embryo**	**Resorption/ implantation** %	**Fetus weight** g
1000 oral	*10,0*	*9,8*	*2,0*	*2,2*
500 oral	*13,4*	*12,4*	*7,5*	*2,1*
50 i.p.	*12,8*	*11,2*	*13,2*	*2,2*

Study of mutagene activity

The mutagene activity of humic acids were studied mainly in AMES tests. The experiments carried out with different microorganisms in different laboratories exclude any kind of mutagene effects (8,10,11).

During the experiments in several cases it turned out that humic acids decrease the mutagene affects of some toxic molecules (10.).

From the results of the toxicologycal studies of humic acids we may conclude that they are non-toxic molecules in the animal and human system.

The protective effects of humic acids against other toxins and heavy metals will be mentioned in the next part.

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