



DRUG DEVELOPMENT

The Pharmacological Properties of the Complex Plant Remedy of Traditional Medicine

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Abstract

The aim of this study was to get an experimental estimation of the anti-inflammatory and immunomodulating properties of the complex plant remedy. The subject of this study was complex plant remedy that has been developed based on the recipes of Tibetan medicine. Experiments were conducted on Wistar rats and male mice of the CBA genetic strain. The anti-inflammatory properties of the remedy were estimated based on the anti-exudative, anti-proliferative and anti-alterative activity, immunomodulating properties on the state of the cell and the humoral chains of the immune response. The remedy tested in this study suppressed the development of formalin-induced edema, reduced the degree of tissue destruction caused by the flogogenic agent and activated the regenerative processes in the seat of inflammation; it also increased the index of the reaction of delayed hypersensitivity and the number of antibody-producing cells. A study of the pharmacological activity of the complex plant remedy indicates that it has anti-inflammatory and immune modulating effects, which are attributable to the complex of biologically active substances.

Key words: complex plant remedy, anti-inflammatory and immunomodulating properties.

Introduction

In the traditional Eastern Asian medical systems, including those of Tibet, a disease is understood as a disturbance in the functioning of the whole body; therefore, therapy is aimed at regulating the structural and functional organization of the body as an entity. Such a position substantiates the use of multicomponent plant remedies in the pharmacotherapy of various diseases [1].

Complex plant remedies certainly possess some advantages over single-component preparations. In particular, they have a versatile effect on the body due to the complex and balanced chemical composition and rational combination of biologically

active substances. On the one hand, they directly influence the seat of injury, while on the other they provide a pharmacological correction of the various functional systems, as well as increase the resistance of the whole body. Besides, the plants when used in combination are observed to manifest synergism, strengthening the beneficial properties of the ingredients included in their composition. In contrast to xenobiotics, biologically active substances of different chemical groups found within the plants bestow not only their polyvalent effect and complex influences but also a maximal biological accessibility [2]. These properties provide a more gentle effect, high degree of efficiency, good tolerance and the absence of side effects when the plant preparations are used over long periods of time.

A series of experimental and clinical studies regarding the research on the pharmacological activity of multicomponent plant remedies prepared on the basis of the Tibetan medicine formulae are published in scientific works [3]. In this connection a plant multicomponent remedy developed based on the original formula described in the treatise on Tibetan medicine “Zhud - shi” is of great interest [4].

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The present study, therefore, was aimed at an experimental estimation of the anti-inflammatory and immune modulating properties of the complex plant remedy.

Material and Methods

The subject of the study was complex plant remedy, prepared based on the formulae taken from the "Zhud-shi" [4]. The plant material was identified according to the "Album of Tibetan Paintings" – "Bri sha" and the "Encyclopedic Dictionary of Mongolian Medicine".

The given remedy includes *Calendula officinalis L* (flowers), *Crataegus sanguinea Pall* (fruits), *Scutellaria baicalensis Georgi* (roots), *Myristica fragrans Houtt.* (seeds), *Malus baccata (L.) Borkh.* (fruits), *Rhamnus davurica Pall.* (bark), *Valeriana officinalis L.* (roots), *Glycyrrhiza uralensis Fisch.* (rhizomes), *Rosa* sp. (flowers and fruits), *Cetraria islandica (L.) Ach.* (blastema) and others.

The experiments were carried out on Wistar rats with an initial weight of 170-190 g and male mice of the CBA genetic strain with an initial weight of 18-20 g. The animals were maintained on the standard conditions of the vivarium, and subjected to the same diet and care, light and temperature regimen; the animals were allowed *ad libidum* tap water. Experimental studies were carried out according to the Regulations of the European convention concerning the protection of vertebrates used for experimental and other scientific purposes (Strasburg, 1986).

The remedy tested in the form of a decoction was introduced intragastrically in the dose of 1 ml/100 g of body weight, once a day, during the whole duration of the experiment. *Caleflonum* was used as the preparation of comparison, which was introduced at a dose of 100 mg/kg in line with the same scheme; the control group of animals received the same volume of distilled water.

The anti-inflammatory properties of the remedy were estimated based on the anti-exudative activity observed in the model of aseptic inflammation including the oncometric difference in edema manifestation. The influence of the plant remedy in the proliferative phase of the inflammation was estimated, including the degree of fibrous-granulated tissue formation. The influence of the plant remedy in the processes of alteration was studied estimating the area of necrotic tissue [5].

The reaction of the cell chain of the immune response was studied to estimate the reaction of delayed hypersensitivity against the background of azatioprine immune deficiency induced by sensitization of the mice with sheep erythrocytes.

The humoral chain of the immune response was thus estimated, including the number of antibody-producing cells using the method of local hemolysis [6].

All the data was processed employing the variation statistical methods using the software Statistica for Windows 6.0. For data with normal distribution, inter-group comparisons were performed using student's t-test.

Results and discussion

Research on the anti-inflammatory properties of the plant remedy has established that the tested remedy possesses a marked anti-exudative activity, suppressing the development of formalin-induced edema by 53% as compared with the data in the control and surpassing the effect of the preparation of comparison (Table 1).

Table 1.

Influence of phytoremedy on exudative phase of inflammatory process in white rats

Groups of animals	Volume of aqua, ml	Suppression of edema, %
Control	0.60± 0.05	-
Phytoremedy	0.28± 0.03*	53
Caleflonum	0.45± 0.04*	25

Note: * $p \leq 0.05$ compared with the control group.

In the next series of experiments conducted, the influence of the plant remedy in the processes of alteration in the seat of inflammation was studied, when the first infusion of the tested remedy was given one hour before the introduction of flogogene, and then once a day during the whole course of the experiment. The remedy given demonstrated a marked anti-alterative effect, diminishing the degree of tissue destruction caused by the flogogenic agent and activating the regenerative processes in the seat of inflammation. By the 7th and 14th days, the area of necrosis was 36% and 41% less, respectively, when compared with the control group data. The plant remedy demonstrated the most marked anti-inflammatory effect by the 21st and 25th days of the experiment; in these periods the area of the ulcer injury was 45% and 44% less than in the control (Table 2).

Table 2.

Influence of complex phytoremedy on alterative phase of inflammatory process in white rats

Groups of animals	Area of alteration, cm ²			
	7 days	14 days	21 days	25 days
Control	4.64±0.41	3.72± 0.36	2.34± 0.22	1.89± 0.16
Phytoremedy	2.98± 0.27*	2.22± 0.15*	1.30± 0.14*	1.06± 0.11*
Caleflonum	2.09± 0.14*	2.34± 0.16*	1.09± 0.14*	1.00± 0.09*

Note: See Table 1.

The study of the influence of the tested remedy on the proliferative processes in inflammation revealed that the mass of dry granulomas was 6% more than in the rats of the control group. The medium mass of wet and dry granulomas in the rats receiving the plant remedy barely exceeded the given indices in the rats of the control group and the group of comparison. Therefore, we suggest that the tested remedy has no stimulating effect on the proliferation processes in the seat of inflammation (Table 3).

Table 3.

Influence of the complex phytoremedy on the proliferative phase of the inflammatory process in white rats

Groups of animal	Mass of wet granulomas, mg	Mass of dry granulomas, mg
Control	253±20.6	49.4±2.5
Phytoremedy	319.0±30.6	52.6±4.5
Caleflonum	232.5±17.0	43.1±2.0

Note: See Table 1.

The close interrelation of the inflammation process and the immune system warranted further studies. A study of the cell chain

of the immune response in the control group of mice indicated that azatioprine immune depression was followed by the suppression of the reaction of delayed hypersensitivity by 33.87% when compared with those in the intact group of animals. At the same time, the use of the tested plant remedy increased the index of the reaction of delayed hypersensitivity by 54% in mice receiving the remedy against the background of the above mentioned immune suppression when compared with the control (Table 4). The data obtained revealed that the introduction of azatioprine triggered

Table 4.
Influence of the phytoremedy on the cell chain
of the immune response of mice

Groups of animals	Index of the reaction of delayed hypersensitivity, %
Intact	21.49 ± 1.64
Control (azatioprine + aqua)	14.21 ± 0.91
Phytoremedy + azatioprine	22.02 ± 1.50*

Note: See Table 1.

a decrease in the absolute as well as the relative number of antibody-producing cells by 57% when compared with the data of the intact group.

The introduction of the tested plant remedy against the background of immune suppression was followed by a 1.8 and 1.4 times increase in the number of antibody-producing cells in the absolute means, as well as in terms of 10^6 splenocytes, respectively, when compared with the data from the animals of the control group (Table 5).

Table 5.
Influence of the phytoremedy on the humoral chain
of the immune response in azatioprine immunosuppression in mice

Groups of animal	Absolute number of antibody-producing cells	Number of antibody-producing per 10^6 splenocytes
Intact	97559.1 ± 7256.2	751.7 ± 55.7
Azatioprine + aqua	42947.5 ± 2852.9	323.2 ± 30.4
Phytoremedy + azatioprine	81258.2 ± 3475.3*	466.22 ± 35.8*

Note: See Table 1.

Conclusion

Thus, this study of the pharmacological activity of the complex plant remedy indicates that it does possess an anti-inflammatory and an immunomodulating effect. The anti-inflammatory effect is characterized by the marked anti-exudative activity, which is proved by the significant decrease in the degree of the exudative processes in the model of formalin-induced edema. Besides, the tested remedy demonstrates a protective effect on the development and reduction in the area of necrotized tissue, resulting in a regeneration of the injured tissue, however, with no influence on the proliferative phase of inflammation. Stimulation of the cell chain of immunity along with the increase in the index of the delayed hypersensitivity reaction and humoral chain of immune response coupled with the increase in the number of antibody-forming cells in the azatioprine immune suppression accounts for the immunomodulating activity of the tested plant remedy.

The revealed pharmacological activity of the multicomponent plant remedy is attributable to a complex of components which supplement and stabilize each other, such as flavonoids, tannins, ether oils, mucilage and tars [7, 8]. The wide spectrum of biologically active substances evolutionally established as protective systems is assumed to promote the realization of the anti-inflammatory and immunomodulating properties of the tested remedy. A favorable combination of the given pharmacological properties in the plant remedy allows its usage for anti-inflammatory as well as immunomodulating purposes in chronic inflammations against infections and to increase the general resistance of the body.

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