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THE ANTI INFLAMMATORY EFFECTS OF A HYDROGEL FORMULATION WITH BEE VENOM

Adriana DĂRĂBAN,[1*] Magda MITITELU[2], Gheorghe DEHELEAN[1]
[1]"Vasile Goldiş" Western University of Arad, Romania
[2]UMF Carol Davila

ABSTRACT. A new gel formulation containing bee venom and propolis tincture was prepared for testing the anti inflammatory effect on edema induced on rat leg by two different edemogen substances. Two experimental methods for the determination of anti inflammatory effects was studied concerning the influence of different edemogen substances on inflammatory effusion of induce edema on the rat leg. The mechanism orientations can also be predicted.

Keywords: new anti inflammatory gel formulation, bee venom, propolis

MATERIALS AND METHODS

The new anti inflammatory gel has made by mixing the following componets (p/100p):

Carbopol 940	1,5
Glicerine	3
10% NaOH solution	3
Propolis tincture	2
Chili pepper tincture	2
Essential pine oil	1
Bee venom	0.05
Preserving agent	87.45

Carbopol was triturated with glycerin and then preserving agent was added and homogenized. The resulted mixture was neutralized by a 10% NaOH solution. After neutralization, the mixture was keep 24 hours for complete gelification.

In this carbocol gel the following were aded: propolis tincture and and chili pepper tincture, by trituration, then the essentiall pine oil until homogenization. The bee venom was separtely dissolved in preserving agent, then was added and triturated with the first mixture.

The advantages of the new gel formulation are the following:

- the new association of the natural biological principles with antimicrobial and antifungal effects gives a very good stabilization to the new gel formulation;
- anti inflammatory and repulsive effects very intensive and quickly;
- an imunomodulator effect by nonspecific mechanisms;
- an anesthesia effect from the first utilization;
- a peripherally circulation activating by some natural components;
- a synergic effect due to combination of propolis tincture and bee venom.

The new anti inflammatory gel formulation proved that the synergic effects of natural active biologically compounds may give new perspectives for the natural treatments of rheumatically affected or anti inflammatory from different origins. Not only this facts proved the efficiency of this new gel formulation but also the benefices on peripheral circulation too. Neither synergic effects of such natural compounds were put to work for the benefices on human health.

The propolis tincture was obtained by extraction from natural propolis as described below: 30 g propolis was treated with 100 ml ethylic alcohol and then, after a week at room temperature and in the dark, the tincture was separated by filtration.

The chili pepper tincture was a hydro alcoholic extract of *Capsicum annuum*, from the ***Dacia Plant***. The composition of this extract given by ***Dacia Plant***: alkaloid (capsicum), caratenoides, flavoinedes, volatile oils, vitamins (A, B, C, PP), macro- and microelements (K, S, P, Mg, Na, Fe, Mn, Cu, Co).

For the pine essential oil, a product of Hofigal was used, product obtained from Pinus silvestris, Fam. Pinaceae by water vapors methods. The essential pine oil is welknown as good healing for the osteoarticular, muscular, rheumathical, artritis etc. deseases.

The bee venom was certified before use, as it is shown from the certificate presented below:

**Correspondence: Adriana Dărăban, "Vasile Goldiş" Western University of Arad, Romania*
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AUTORITATEA NAȚIONALĂ PENTRU CERCETARE ȘTIINȚIFICĂ
INSTITUTUL NAȚIONAL DE CERCETARE-DEZVOLTARE
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Calea Vitan 112, COD 031299 București Sector 3 ROMÂNIA
Înregistrat la Of.Com. J40/963/1997
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TEL: +40-21-321.21.17; +40-21-321.62.10; +40-21-322.29.10
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Rezultate:

Denumire parametru	Cerinta	Rezultat analiza	Concluzia
Aspect	Pulbere microcristalina	Pulbere microcristalina	Corespunde
Culoare	Alb pana la bej	Alb galbui	Corespunde
Solubilitate	Usor solubil in apa	Usor solubil in apa	Corespunde
Aspect solutie	Solutie usor opalescenta	Solutie usor opalescenta	Corespunde
Continut proteine (Lowry)	75-88%	79.23%	Corespunde
Electroforeza (Analiza pe chip "Protein 230")	Aspect specific, prezenta markerilor, benzi bine definite	Aspect specific, prezenta markerilor, benzi bine definite – Anexa A	Corespunde

Concluzii: Proba Venin de albine este corespunzatoare din punct de vedere calitativ

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Two experimental methodes were used for the edema induced as acute inflamatory: one concern with a 10% caolin suspention and the second vith a dextran 10% solution, both applied on rat leg. (Cristea E., et al., 2002; Mihele D., et l., 2005; Mogoşan C., et al.,2000; Mihele D., et al., 2003;). The edema were induced by intraplantar of 0.1 mL caolin suspention, respectively 0.2 mL dextran 6% solution.

For each edemogen agent three groups, 10 Wistar male rats, about 170±15 g, were used. One of the groups was the control group, the second one was treated with a 4% phenilbutazone gel, based on carbacol 1%, and the last group was treated with new anti inflamantory gel composition.

Too all rats the edemogen agent were applied. On the leg that the edema was induced, the anti inflammatory agent was applied uniformly, in thin layer, about 0.25 g, exception of the control group.

The volume of rat leg was pletismometric measured after the intraplantar injection of the edemogen agent. The pletismometric measurements were made for different intervals: 2, 4, 6 and 24 hours, for 10% kaolin

suspension, and 30, 60, 90 and 120 minutes for the 6% dextran solution, respectively.

The medium value of anti inflammatory, in mL, was calculated, the standard error and the edema inhibition, too, for each group of rat, as:

edema inhibition, % = (1-X substance / X control) x 100

were:

- X substance is the medium value of induced edema for each tested substance
- X control is the medium value of induced edema for each, determined to similar intervals as in tested substances.

The statistical evaluation was made using the Student test (Simionovici M., et al., 1983; Joean D. 1997).

RESULTS AND DICUSSIONS

The new formulated gel has after 2 hours an anti inflammatory effect about 51.26% lower as 10% caolin suspension, and a 70.65% lowering for the 4% phenylbutazone gel, after 4 hours, respectively. (Table 1) The efficiency of new gel formulation is well outline from these data.

Table 1. The anti inflammatory effect of new gel formulation and phenylbutazone gel on inflammatory edema induced by a 10% caolin suspension

tested product	Edema 2 h (mL) ($\bar{X}$ ± SD.)	Edema 4 h (mL) ($\bar{X}$ ± SD.)	Edema 6 h (mL) ($\bar{X}$ ± SD.)	Edema 24 h (mL) ($\bar{X}$ ± SD.)
Control	0,238 ± 0,01	0,276 ± 0,03	0,340 ± 0,02	0,293 ± 0,01
New anti inflammatory gel	0,116 ± 0,04**	0,143 ± 0,01**	0,184 ± 0,03**	0,172 ± 0,02**
Effect %	-51,26	-48,18	-45,88	-41,29
Phenylbutazone gel	0,098 ± 0,01**	0,081 ± 0,03**	0,105 ± 0,02**	0,104 ± 0,04**
Effect %	-58,82	-70,65	-69,11	-64,50

$\bar{X}$ ± SD = media ± standard deviation; **p<0,05.

Fig 1. The evolution of new gel formulation and phenylbutazone on inflammatory edema induced by a 10% caolin suspension

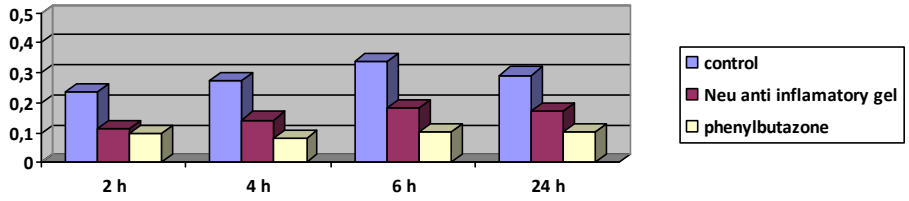
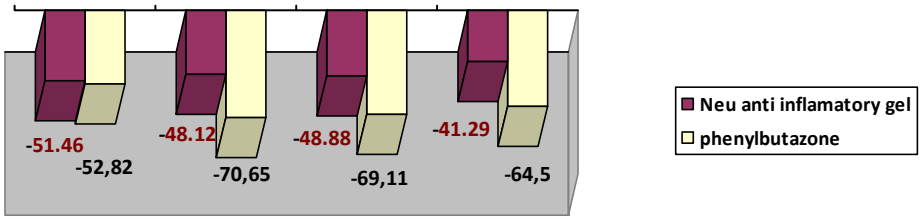


Fig 2. The anti inflammatory efect of new gel formulation and phenylbutazone on inflammatory edema induced by a 10% caolin suspension



For the experimental edema produced by 6% dextran solution the new anti inflammatory gel formulation has the most power effect after 90 min, about 58.12%; for phenyl butazone gel the most power effect after 30 min, about 72.41%, respectively. (Table 2.)

Table 2. The anti inflammatory effect of new gel formulation and phenylbutazone gel on inflammatory edema induced by 6% dextran solution

tested product	Edema 30 min (mL) ($\bar{X}$ ± SD.)	Edema 60 min (mL) ($\bar{X}$ ± SD.)	Edema 90 min (mL) ($\bar{X}$ ± SD.)	Edema 120 min (mL) ($\bar{X}$ ± SD.)
Control	0,203 ± 0,02	0,227 ± 0.02	0,252 ± 0,03	0,265 ± 0.03
New anti inflammatory gel	0,085 ± 0,01**	0,110 ± 0,01**	0,131 ± 0,01**	0,141 ± 0,01**
Effect %	- 58,12	-51,54	-48,01	- 46,79
Phenylbutazone gel	0,056±0,04**	0,065 ± 0,01**	0,076±0,02**	0,074 ± 0,01**
Effect %	- 72,41	-71,36	-69.84	-72,07

$\bar{X}$ ± SD = media ± standard deviation; **p<0,05

Fig 3. The evolution of edema inflammatory edema induced by a 6% dextran sulution

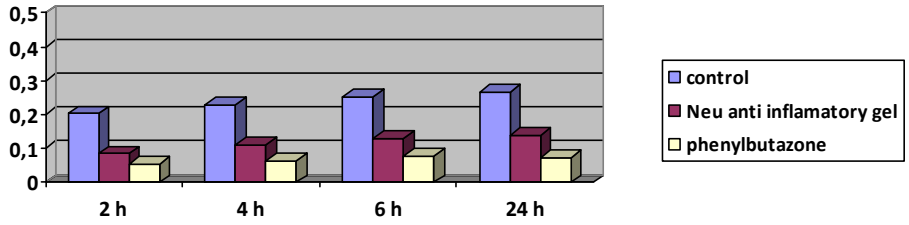
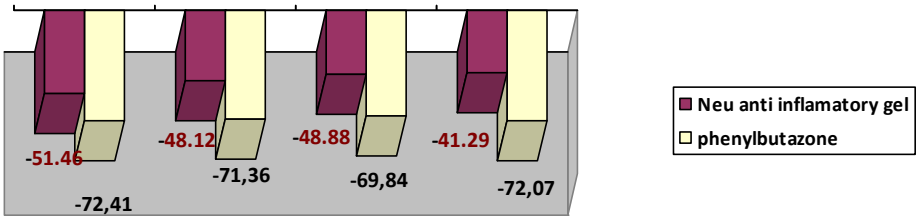


Fig 4. The anti inflammatory efect of new gel formulation and phenylbutazone on inflammatory edema induced by a 6% dextran solution



CONCLUSIONS

The data presented in Table 1. and Table 2. confirm the good proprieties of anti inflammatory new gel formulation base on bee venom and propolis. New modification to this composition may give better results.

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