MUCO-ADHESIVE HAEMOSTATIC GEL WITH POLYURONIDES FOR ENDONASAL ADMINISTRATION

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Our investigations have considered (1) the preparation of a muco-adhesive gel on a base of polygalacturonic acids existing in pectin extracted from quince, using an original process (1) and the testing of its availability, and (2) the assessment of its haemostatic effect.

The use of pectins as haemostatic agents was reported in Romania in 1958 by Ionescu-Stoian et al. (2), who demonstrated by pharmacological experiments in rats that pectin, administered intravenously, reduced the bleeding time (BT) by 50%, in a quantity of 0.001 g/kg body weight.

Material and methods
Preparation of the muco-adhesive gel and determination of its availability.

In view of the pharamacological efficiency of the combination of pectins with different macromolecular substances, the pectin obtained as a hydrolysis product in an acidic medium using fruits of Cydonia vulgaris was combined with a bivalent cation (Mg^{2+}) in the form of magnesium glutamate (2.6%). The combination of the pectin hydrogel (Pectogel) (PG) with other hydrogels was carried out in the ratio 1/1. The inclusion of the cation was based on the research results (4, 5, 6) which demonstrate the cytoprotective effect, and the stopping of wounds in muco-cutaneous therapy, and the anti-herpetic, decongestive, osmotic and anti-inflammatory effect.

The dialysis method (7) was used to evaluate the dynamics of the transfer of the cation from the mixed Pectogels and uncombined hydrogels. Magnesium was determined quantitatively by the complexonometric method (B), by daily sampling of specimens for six days ($37\pm0,1^{\circ}C$). The total quantities comparatively transferred are shown in Table 1.

Results and discussion

The results obtained show that the most efficient combination is the 1/1 mixture of 3% pectin gel and 4% methylcellulose hydrogel, prepared in the presence of preservatives (0.075 g% nipagine and 0.025 g% nipasole) with a content of 2.6 weight % of magnesium glutamate.

Table 1

Table 1

Comparative transfer of magnesium (%) from single hydrogels and hydrogels combined with 3% pectin gel (PG)

Hydrogel	Mg^{2+} (%)	Hydrogel with pectin gel 1/1	Mg^{2+} (%)
methylcellulose 4%	61.52	methylcellulose 4% + PG	92.75
carboxymethylcellulose 5%	21.10	carboxymethylcellulose 5% + PG	45.93
hydroxyethylcellulose	82.94	hydroxyethylcellulose 3% + PG	85.13
sodium alginate 3%	40.65	sodium alginate + PG	37.32
bentonite 30%	33.22	bentonite 30% + PG	87.25
polyethylene glycols 400 + 4000 1/1	89.82	polyethylene glycols 400 + 4000 + PG	96.24
pectin 3% + glycerol 10% + water 87%	99.36	pectin 3% + glycerol 10% + water 87%	99.36
reference (2.6% of magnesium glutamate)	98.43		

Assessment of pharmacological effects

The haemostatic effect of the 3% Pectogel was monitored by determining the bleeding time (BT) in rats (110 g, n=20) (2.9). The rats were kept for 2 to 3 min with the tail in the controlled-temperature bath at $38 \pm 0.5^{\circ}C$, and haemorrhage was caused by the incision of the tail at a distance of 2 mm from the apical region. The BT was determined by recording the time from the moment of incision to the production of haemostasis. In Table 2, the result obtained on the batch of control animals, in which no Pectogel was applied, are compared with the haemostatic effect of the product, identified with a quantity of 0.03 g pectin, corresponding to 0.009 g of polygalacturonic acids, where the reduction in BT is 41.70%.

Table 2

Bleeding time (average values) in controls and specimens (s)

parameter	controls	specimen tests
bleeding time (s)	59.95 ± 2.50	34.90 ± 1.0
bleeding time: controls/specimens	1.71	
reduction of bleeding time (%)	41.70	

Conclusions

A formula is developed for the preparation of a muco-adhesive gel containing certain synthetic macromolecular substances (methylcellulose) and natural substances (pectin) and bivalent cation (magnesium).

The pectin in the hydrogel selected displays an obvious haemostatic effect, by reducing the bleeding time by 41.70%.

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The authors' aim was to obtain certain gels based on polygalacturonic acids existing in pectin extracted from quince /Cydonia vulgaris/, using an original procedure with a view to apply them in endonasal therapy as muco-adhesive preparations with haemostatic effect.

The favourable effects pointed out by availability tests were obtained by associating one gel of 3% pectin /Pectogel/ with one gel of methylcellulose hydrogel /1:1/ in the presence of 2.6% magnesium glutamate with cytoprotecting and anti-inglammatory effect, -an association selected from 8 preparations. The pharmacological tests in rats revealed the haemostatic effect of Pectogel, which reduces the time of coagulation by 41.70% as compared with the controls.