To the pharmacology of "Saint John's herb" (St. John's wort Hypericum perforatum perforatum).

Message 4: Comparative assessment of the impact of St. John's wort on education toxic-dystrophic erosions of the stomach and healing of necrosis O.D. Barnaulov

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Pharmacological properties of St. John's wort (Hypericum perforatum). The 4threport: the comparative estimation of Hypericum preparation influence on the appearing of toxico-dystrophic gastric erosions and healing of gastric necrosis

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SUMMARY

Infusions from the aerial part of St. John's wort and 3. tetrahedral at a course (7 days) preventive enteral administration were equally effective in reducing the destructive effect of non-steroidal anti-inflammatory drugs on the gastric mucosa in rats. Dealcoholized tincture of ginseng root showed higher antidestructive activity. These phytopreparations, when administered preventively, limited the area of gastric necrosis in mice caused by the injection of an acetic acid solution. With therapeutic administration, the healing of necrosis was accelerated.

Keywords: phytopharmacology, kinds Hypericum, anti-destructive, gastroprotective, healing activity.

RESUME

The preventive (for 7 days) enteral introduction of herbal infusions of Hypericum perforatum or H. quandrangulum demonstrated equal effectiveness in lowering nonsteroidal antiinflammatory remedies destructive action on the rat's gastric mucous membrane. The Panax ginseng root dealcoholized tincture manifested more high antidestructive activity. These phytopreparations introduced enteraly decreased areas of gastric necrosis provoked by acetic solution injection in mice and accelerated necroses healing when introduced curatively.

keywords:phytopharmacology, Hypericum species, anti-destructive, gastroprotective and healing activity.

INTRODUCTION

Previously, the results of a comparative assessment of the wound healing activity of various extracts from two types of St. John's wort [1], both for local and enteral application, were reported. The highest activity is shown by water extracts from the aerial part, which corresponds to the tradition of using the infusion, "St. In traditional Iranian-Tajik medicine, St. John's wort, among other things, is considered an antiulcer agent [2]. In this regard, it is of interest to evaluate and compare the gastroprotective activity of infusions (that is, the most used extemporaneous medicinal forms) of the two most common types of St. John's wort, which are not distinguished among the people. The widest, sometimes The misuse of numerous non-steroidal anti-inflammatory drugs (NSAIDs) has posed the most urgent task for doctors: the prevention of side effects, for example, their gastrotoxic effects. Exacerbations of peptic ulcer, erosive gastritis, gastric

bleeding, just dyspeptic disorders (heartburn, belching, nausea) are well-known complications of NSAID treatment. However, detoxification therapy is almost never prescribed in parallel, the best option of which is herbal medicine [3]. The formation of a new discipline - detoxifying herbal medicine should be supported by both experimental and, in particular, clinical research. In the presence of clinical experience in leveling the toxic effect of various synthetic drugs with infusions of polycomponent plant collections [4], it was still of interest to clarify the legitimacy of including St. John's wort species in them. For this purpose, classical NSAIDs were used, the ability of which to cause erosion of the secretory part of the stomach has long been used in the experiment.

The interpretation of erosions caused by atophane, butadione, indomethacin as a model of peptic ulcer does not stand up to criticism. These erosions, without any positive intervention, are literally epithelialized within a few days, and it is impossible to monitor their healing. Histological studies confirm the superficial nature of these lesions, the absence of damage to the muscle layer [5]. For this reason, it is more correct to use the proven method of introducing a solution of acetic acid or ethanol under the serous membrane of the secretory part of the stomach, which makes it possible to trace a decrease in the area of infarct-like, full-thickness necrosis of the stomach for almost a month. An absolute analogy with human peptic ulcer is also difficult in this case, but this method makes it possible to identify agents that accelerate the healing of destruction [5, 6]. In connection with the above,

MATERIAL AND RESEARCH METHODS

Since the purpose of the research was a comparative assessment of the comparability of the activity of two types of St. John's wort, their interchangeability, we preparedex tempore infusions1:10 from aerial parts collected during the flowering of 3. perforated and 3. tetrahedral H. quandrangulum. These infusions were administered through a tube into the stomach of outbred male white rats (150-200 g) at 5 ml / 100 g or mice at 0.5 ml / 10 g, i.e. in terms of dry raw materials, 5 g/kg for 7 days before the damaging effect. As such, a solution of butadione in acetone was used, which was injected to rats intramuscularly at a dose of 250 mg/kg, or a solution of atofan in dimethyl sulfoxide (300 mg/kg intraperitoneally). After 20 hours, the number of erosions of the secretory part of the stomach was counted, grading them into small (0.5-1.5 mm in diameter), medium (1.5-2.5 mm) and large (2.5-5.0 mm and more).). All erosions are brightly stained with hydrochloric hematin, and therefore their calculation is not difficult. The day before the injections, the animals were deprived of food with free access to water. Methods of damage to the gastric mucosa with the introduction of atofan or butadione, as well as other NSAIDs, are generally accepted. When statistically processing the results according to the criteria t and χ_2 [7] compared in the control (introduction of water through a tube into the stomach for 7 days) the number of animals without erosions, including each type of them, the average number of certain and all erosions per 1 animal in the group, the percentage of erosions of various sizes from their total. The latter indicator makes it possible to note even a weak protective effect in terms of shifting the severity of lesions towards light, small erosions. The method of comparative evaluation of preparations proposed by us makes it possible to rank them according to the level of protective activity [5].

The generally accepted method used for more than half a century for the formation of fullthickness, long-term non-healing necrosis (ulcers) of the stomach in rats by injection of an acetic acid solution under the serosa [5, 6] was modified by us for mice, which allows us to significantly expand the samples at different times for calculating the area of healing necrosis. During a working day, 3 experimenters can operate up to 200 animals. Under ether anesthesia with a microsyringe, 0.006 ml of a 4% solution of acetic acid was injected under the serous membrane of the stomach. acids. The anterior abdominal wall was sutured in layers. The parameters of oval lesions were measured using an eyepiece micrometer under a binocular loupe with an accuracy of 0.025 mm. Infusions of St. John's wort species were introduced in one of the series of experiments preventively for 7 days and then daily from the 3rd day after the operation, and in another series of experiments, when studying the therapeutic effect, only from the 3rd day. Since in preliminary experiments during the development of the method it was found that only on the 3rd-4th day the volume of lesions is completely cleared of necrotic masses and its area does not undergo changes during this time, the control measurement of the initial area was made on the 4th day and was taken as 100 % (Table 3).

The control drug in experiences Withbutadione and atofan served dealgocolized pharmacy tincture 1:10 of ginseng roots at a dose of 1.5 g/kg (in terms of dry raw materials), the anti-destructive effect of which has previously been verified many times [8]. In one of the series of experiments with preventive and therapeutic administration of drugs, the same dealcoholized tincture of ginseng root served as control drugs in experiments with gastric necrosis in mice, and in the other, with therapeutic administration from the 3rd day after surgery, metacil (100 mg / kg), a pharmacopoeial stimulant of regeneration, the solution of which was also administered enterally.

RESULTS AND DISCUSSION

Dealcoholized ginseng tincture showed a strong gastroprotective activity in the model of gastric erosions caused by butadione, which manifested itself in a decrease in the number of animals with small, medium, large and in total with all destructions. The average number of erosions of each caliber and all of them in total was also significantly less than in the control. The number of light, small erosions increased in percentage terms, and, accordingly, the total proportion of lesions of medium and large caliber decreased. All three groups of indicators of the degree of damage to the stomach allow us to consider the ability of ginseng to increase the resistance of its tissues to toxic damage as demonstrative.

The ability to condition SNPS of many other plants, not just classical phytoadaptogens, is currently being widely discussed [2, 3, 8, 10]. The results are given in table. 1, allow us to consider the gastroprotective activity of both types of St. John's wort distinct, close to strong. The preventive course introduction of infusions led to a decrease in the average number of all destructions, including severe, large ones, to a decrease in the number of animals with these lesions. Without analyzing in detail each indicator, I note that none of them showed significant differences between the two types of St. John's wort, and therefore, their interchangeability in folk and traditional medicine is quite legitimate. At the same time, ginseng is significantly superior to St. John's wort, for example, in terms of the average number of all and each type of destruction per animal in the group.

Table 1

Comparative evaluation of the effect of infusions of St. John's wort species on the formation of gastric erosions in rats with the introduction of butadione

drug (amount	Indicators	Number of erosions				
animals in the group)		small	medium	major	Total	
	one	9.9±2.0	1.9±0.6	1.8±0.7	13.6±2.5	
Control (18)	2	72.8	13.8	13.4	one hundred	
	3	0	2	2	0	
Infusion 3. perforated (18)	one	7.4±2.2	1.0±0.4*	0.9 ±0.4*	9.3±2.9*	
	2	79.6	10.8	9.6	one hundred	
	3	3	9*	9*	3	
Infusion 3. tetrahedral (18)		6.3±2.5*	1.6±0.6	0.8±0.4*	8.7±3.3*	
	123	72.4	18.4	9.2	one hundred	
		3	5	9*	3	
Ginseng Root Tincture (15)	one	2.4±1.5*	0.4±0.2*	0.2±0.2*	3.0 ±0.8*	
	2	80*	13.3	6.7	one hundred	
	3	6*	9*	12*	6*	

Notes: 1 - the average number of erosions per 1 animal in the group \pm confidence interval, 2 - the percentage of destruction of their total number, 3 - the number of animals without destruction. * - differences are significant in comparison with the control at p < 0.05-0.01.

Brief comments on the results given in Table. 2. There are no statistically significant differences between St. John's wort species. Formally, the preparations showed the same distinct gastroprotective activity. When using the second technique for obtaining experimental toxic-dystrophic erosions of the stomach, the legitimacy of the equal use of these types of St. John's wort in ethnoyatry and traditional medicines was confirmed. Infusion of 3. tetrahedral is significantly inferior to ginseng in terms of the average amount of all and average destruction. Infusion of 3. perforated showed less pronounced activity in comparison with ginseng in terms of the average number of all and small erosions. The results shown in tables 1 and 2 suggest that interchangeable, equally active types of St. John's wort have adaptogenic properties, the ability to cause SNPS, although in these properties they are inferior to ginseng tincture, which was used in a lower, previously tested [5,8] effective dose: 1.5 g/kg versus 5 g/kg (in terms of dry raw materials). It is obvious that St. John's wort, ginseng can be used to prevent exacerbation of peptic ulcer, to prevent its erosive damage, provoked by frequent and prolonged use of NSAIDs (Table 2).

The problem of preventive phytotherapy does not find its practical implementation. Clinicians are most interested in the effect of various drugs on regeneration, restoration of the morphological integrity of the damaged organ, in our case, the stomach. The section "pharmacology of regeneration", as well as the theory of SNPS, was developed by our most talented compatriot N.V. Lazarev. Thanks to him, targeted syntheses of drugs were carried out that made it possible to cancel deaths in agranulocytosis (tonsillitis, pneumonia), in particular, caused by eating overwintered cereals. So-called regenerative stimulants have come into practice: sodium ribonucleinate, metacil, pentoxyl, potassium orotate. Still, it would be more correct to call them not stimulants, but means that optimize, correct regeneration processes. From the means of traditional medicine, it suggests itself as analogues of mummy, classic adaptogens, a number of other plants: meadowsweet, types of ulcer, plantain, yarrow (cut-grass), many others and, of course, St. The legitimacy of its effective use in the treatment of patients with peptic ulcer can be at least to some extent confirmed experimentally not with superficial erosive, healing in days, but with full-layer necrosis of the stomach. Using the classical method, modified by us for mice, we evaluated the ulcer-healing abilities of St. John's wort in comparison with ginseng in The legitimacy of its effective use in the treatment of patients with peptic ulcer can be at least to some extent confirmed experimentally not with superficial erosive, healing in days, but with full-layer necrosis of the stomach. Using the classical method, modified by us for mice, we evaluated the ulcer-healing abilities of St. John's wort in comparison with ginseng in The legitimacy of its effective use in the treatment of patients with peptic ulcer can be at least to some extent confirmed experimentally not with superficial erosive, healing in days, but with full-layer necrosis of the stomach. Using the classical method, modified by us for mice, we evaluated the ulcer-healing abilities of St. John's wort in comparison with ginseng in

preliminary, prophylactic and subsequent therapeutic administration (Table 3).

table 2

Comparative evaluation of the effect of infusions of St. John's wort species on the formation of gastric erosions in
rate with the introduction of atophane

drug (amount	Indicators				
ulug (alloulit					
animals in the group)		small	medium	major	Total
	one	12.8±5.2	4.5±2.2	4.3±1.8	21.6±6.2
Control (17)	2	53.4	20.7	19.9	one hundred
	3	0	2	4	0
Flask 3. Perforated (15)	one	9.5±3.1	1.5±1.2*	1.7±1.3*	12.8 ±4.1*
	2	74.5*	12.0	13.5	one hundred
	3	4	9*	eight	4
Infusion 3. tetrahedral (15)	one	9.5±4.2	2.2±1.0*	2.0±0.8*	13.7 ±3.5*
	2	68.9*	16.1	15.0	one hundred
	3	3	6	eight	3
	one	5.3±2.6*	0.9 ±0.6*	1.1±0.7*	7.3±3.1*
Ginseng Root Tincture (15)	2	72.7*	12.7	14.6	one hundred
_	3	4	9*	10*	4

Notes: 1 - the average number of erosions per 1 animal in the group \pm confidence interval, 2 - the percentage of destruction of their total number, 3 - the number of animals without destruction. * - differences are significant in comparison with the control at p < 0.05-0.01.

Table 3

Comparative evaluation of the effect of phytopreparations on the area of full-thickness necrosis of the stomach in mice with preventive and therapeutic and only therapeutic enteral administration

drug, single	Area of necrosis in mm2and in percentage terms after the operation:					
dose	For preventive and curative administration					
	4th day	8th day	15th day	20th day	26th day	
Control: water 0 E	10.15 + 3.1	9.96 ± 4.2	3.80±2.4	1.58 ± 1.1	1.49 ± 1.2	
control. water 0.5	100 + 30.5%	98.1±41.3%	37.4±23.6%	13.6±10.8%	14.7±11.8%	
mi/10 g	(eight)	(eight)	(10)	(twenty)	(twenty)	
Infusion 1:10 Z.	7.05 ± 1.50*	5.45 ± 2.1*	1.25 ± 1.2*	0.80±0.4	0.48 ± 0.3*	
perforated by	100±21.2%	77.3±29.8%	17.7±17.0%	11.3±5.7%	6, 8±4.2%	
0.5 ml/10 g.	(eight)	(eight)	(10)	(10)	(10)	
Infusion 1:10 Z.	6, 90 ± 1.4*	5.05 ± 2.3*	2.65±1.8	0.85±0.6	0.42 ± 0.4*	
tetrahedral	100±20.3%	73.2 ± 33.3%	38.4±6.1%	11.3±8.7%	6.1±5.8%	
0.5 ml / 10 g.	(eight)	(9)	(10)	(10)	(eleven)	
root tincture	6, 12 ± 1.7*	3.45 ± 1.1*	1.15 ± 0.7*	0.65 ± 0.3*	0.25 ± 0.2*	
ginseng 1:10's	100±27.8%	56.4±18%*	18.8±11.4%	10.6±4.9%	4.1±3.2%*	
0.15 ml/10 g	(eight)	(eight)	(10)	(10)	(10)	
	Only for therapeutic use					
Control: water 0.5	12, 29 ±5.53	8.92 ± 3.77	5.62 ± 1.90	1.75 ± 1.22	1.24 ± 1.05	
ml/10 g	100±45%	72.6 ± 30.7%	45.7±15.5%	14.2±9.9%	10.1±8.5%	
	(10)	(10)	(10)	(twenty)	(twenty)	
Infusion 1:10 Z.	13.40±5.82	9.02 ± 4.45	3.01 ± 1.40*	0.72 ± 0.42*	0.45 ± 0.22*	
perforated by	100±43.4%	67.3±33.2%	22.5±10.4%*	5.4±3.1%*	3.4±1.6%*	
0.5 ml/10 g	(10)	(10)	(10)	(twenty)	(21)	
Infusion 1:10 Z.	11.85 ± 4.39	6.77 ± 2.83*	2.95±1.22*	0.75 ±0.32*	0.35 ± 0.18*	
tetrahedral	100±37.0%	57.1±23.9%*	24.9±10.3%*	6.3±2.7%*	3.0±1.5%*	
0.5 ml / 10 g.	(10)	(10)	(10)	(twenty)	(23)	

	12.85±5.15	5.87 ± 2.35*	2.05±1.42*	0.72 ± 0.36*	0.22 ± 0.12*
Metacil 100 mg/kg	100±40.0%	45.7±18.3%*	16.0±11.1%*	5.6±2.8%*	1.7±0.9%*
	(10)	(10)	(10)	(twenty)	(twenty)

Notes: mean values are given \pm confidence interval; * - differences with control are statistically significant at p < 0.05-0.01; the number of animals in the group is given in parentheses.

The somewhat unexpected results obtained, from our point of view, are of significant importance as an experimental confirmation of the validity of the SNPS theory. It was assumed that the preventive administration of drugs would not significantly affect the initial size of necrosis obtained with such a hard impact, but the latter, against the background of all 3 drugs, already on the 4th day before the start of active regeneration processes were significantly smaller than in the control. The anti-destructive component of SNPS, the mobilization of defense mechanisms led to a decrease in the volume of lesions. Previously, similar results were obtained by us for various plants when hepatocytes were damaged by carbon tetrachloride, ßcells of the islets of Langerhans of the pancreas were damaged by alloxan, and conditioned and unconditioned reflex behavior of animals by electric current [5, 8, 10]. Hence, the ability of phytopreparations to limit not only the stage of exudation and proliferation (background antiinflammatory activity for plants), but also the stage of alteration, to have an anti-destructive effect is a universal property that does not depend on the nature of the damaging effect. So, in the experiments of V.V. Vorob'eva [11], plant metabolites minimized the damaging effect of vibration and chemical agents. The universality of antidestructive activity is not of the organ and tissue, but of the organism scale. This property of many medicinal plants is essential in the treatment of patients with chronic diseases with unpredictable exacerbations: exacerbations of multiple sclerosis, acute disorders of cerebral and coronary circulation, exacerbations of nonspecific ulcerative colitis, atopic bronchial asthma, paroxysms of tachycardia, arrhythmias, convulsions,... So, with reference to the tradition of using St. John's herb in cases of brain disease, the effectiveness of hyperforin and (remarkably) a complex extract 3. perforated in limiting cell infiltration (anti-inflammatory action), demyelination, axonal degeneration, autoimmune aggression (anti-destructive action). The recommendation of the authors to use St. John's wort for PC reinforces our effective inclusion of the plant in collections for this pathology [13]. Since the importance of inflammation in the pathogenesis of MS has long been proven, experimental confirmation of the anti-inflammatory activity of St. John's wort species, in particular H. oblongifolium, is essential [14]. Not only with this

Obviously, in the presence of such starting advantages as an initially smaller volume of lesions, the area of necrosis on the background of herbal medicine was subsequently significantly less than in the control. Ginseng, except for the 15th day, had no significant advantages in comparison with St. John's wort. Only with therapeutic, rather than preventive, use of metacil and phytopreparations (Table 3), the initial area of necrosis was almost the same in all groups. The positive effect of drugs on the healing of necrosis was similar, and there were no statistically significant differences between them. Considering the disproportionately lower economic costs in the treatment of St. John's wort infusions in comparison with metacil and many other medicines, both therapeutic and, in particular, prophylactic use of "St. John's wort tea" should be promoted. However, own clinical experience allows us to expand this recommendation to the use of polycomponent teas for peptic ulcer and erosive gastritis: St. Expansion of the composition of the collection due to mint, lemon balm, oregano, plantain, black currant leaf, strawberries will not be

mistake. Prophylactic intake of such teas avoids recurrence, exacerbation of peptic ulcer, erosive gastritis provoked by medication, and has an undoubted restorative effect, judging, for example, by a sharp decrease in the frequency and complete absence of acute respiratory viral infections.

CONCLUSIONS

1. Infusions of the aerial parts of St. John's wort and 3. tetrahedral exhibit equal antidestructive activity in the model of erosions of the secretory part of the stomach in rats caused by non-steroidal anti-inflammatory drugs (NSAIDs), but inferior to ginseng tincture in a number of indicators.

2. The legitimacy of the use of St. John's wort, ginseng preparations for the prevention destructive effect of NSAIDs on the gastric mucosa has been experimentally confirmed.

3. Preventive administration of St. John's wort and ginseng reduces the area full-thickness necrosis of the stomach caused by the injection of a solution of acetic acid under the serous membrane, and their therapeutic use accelerates the healing of necrosis, which confirms the legitimacy of the use of St. John's wort for peptic ulcer disease.

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