REVIEW

ALTERNATIVE THERAPIES IN GASTRIC HYPERSECRETION

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Abstract

In addition to its advantages (technological progress, high-performance medical treatment, multiple information sources, new communication systems), the 21st century brings many disadvantages, such as: professional stress due to the uncertainty of the future and to the increasingly higher professional performance indicators, the quality of interpersonal relationships, an imbalance between professional and personal life, a lack of interest in self-knowledge. Besides all these stress factors, certain drugs, inadequate nutrition both in terms of quantity and quality, a small number of meals eaten per day, a late last meal, as well as late bedtime cause an increase of gastric secretion. Depending on the psychosomatic profile of patients, these can be divided into two main categories: patients who accept drug therapy and patients who prefer alternative therapies. This review aims to present all types of alternative therapies, for which preclinical studies are available.

Rezumat

Pe lângă avantajele secolului XXI (progresul tehnologiei, tratamente medicale performante, surse multiple de informații, noi sisteme de comunicare), acesta aduce și numeroase dezavantaje, ca de exemplu: stresul profesional datorat nesiguranței zilei următoare, a indicatorilor profesionali de performanţă tot mai ridicați, calitatea relațiilor interpersonale, dezechilibrul între viața profesională și cea personală, lipsa de interes a cunoașterii de sine. Pe lângă toți acești factori de stres, anumite medicamente, alimentația necorespunzătoare, atât din punct de vedere al cantității, calității, numărului mic de mese servite într-o zi, ora târzie de servire a ultimei mese, precum și ora târzie de culcare, duc la creșterea secreției gastrice. În funcție de profilul psihosomatic al pacienților, aceștia pot fi împărțiți în două mari categorii: pacienți care acceptă tratamente medicamentoase și pacienți care preferă terapii alternative. În acest sens, prezentul articol încearcă prezentarea tuturor tipurilor de terapii alternative pentru care există studii preclinice.

Keywords: alternative therapies, gastric hypersecretion, phytotherapy

Introduction

Over the past years, the incidence of gastrointestinal diseases has continuously increased in Europe, and particularly in Eastern Europe. The most frequent gastric disorders are upper digestive haemorrhage, Barrett's oesophagus, esophagitis, eosinophilic esophagitis, gastroesophageal reflux disease, and *Helicobacter pylori* infection [11]. For their treatment, numerous drugs have been developed, such as: anti-secretory agents – histamine (H_2) receptor blockers, antacids, proton pump inhibitors (PPIs), prokinetics or topical drugs for mucosal protection. Although PPIs are the most effective in the treatment of these diseases, due to their adverse events or reactions (e.g. hypersensitivity reactions, iron deficiency anaemia, increased risk of fractures, hypomagnesemia and B_{12} vitamin deficiency, acid-base imbalance), but also due to the fact that many patients do not respond to PPIs treatment, there is an increasingly high number of patients who prefer alternative therapies.

Alternative therapies used for the treatment of gastric secretion are: acupuncture, phytotherapy, breathing exercises, acupressure, hypnotherapy, electromagnetic resonance, and electro-acupuncture. Also, in the treatment of gastroesophageal reflux, relaxation as a psychological factor and lifestyle changes have been applied.

In recent years, increasing clinical and preclinical evidence in favour of phytotherapy has been obtained. Another promising alternative therapy is represented by special nutritional food products. According to Directive 2009/39/CE of 6th May 2009, changed and/or completed, this type of food products will be designed and produced to meet the special nutritional needs of persons for whom they are mainly intended. Thus, these persons may have disturbed digestive or metabolic processes or a certain physiological

condition, and they can particularly benefit from the controlled consumption of certain substances in these foods. According to the Directive, these food products can be characterized as "health food" of "diet food". This study reviews alternative phyto-therapeutic treatments and the results obtained in preclinical studies.

Materials and Methods

The PubMed, Medline, SpringerLink, EbscoHost and Elsevier databases were searched for preclinical studies, and articles published in all languages in the period 1996-2015 were selected. The search terms used were the gastroprotective effects of phytotherapy in mice, Wistar rats, rabbits and cats.

Results and Discussion

The results of the analysis of phytotherapeutic treatment used in preclinical studies are shown in Table I.

Table I

Phytotherapy used in preclinical studies for the treatment of gastric secretion

Phytotherapeutic remedy, bibliographic source	Preclinical study			Main action monitored and demonstrated
	Rabbits/Cats	Mice	Rats	
Acacia ataxcantha (methanolic leaf extract), [2]	-	-	X	Increase of gastric pH
Aparisthmium cordatum (extract), [17]	-	X	X	Antiulcerogenic activity of the diterpenoid aparisthman: gastric acid ↓, mucus production ↑, prostaglandin synthesis ↑
Artocarpus obtusus Jarret (extract), [10]	-	-	X	Gastric mucosal protection through: MDA ↓, GSH ↓, NO ↓, COX-2 – inhibition
Bacopa monniera Wettst (fresh juice), [30]	-	-	X	Gastric mucosal defensive factors
Benincasa hispida (fruit juice), [44]	-	-	-	Efficiency in dyspepsia
Berberis lyceum (raw extract and methanolic extract), [25, 42]	X	X	-	Mediation of the spasmolytic effect through Ca^{2+} channels
Bidens aurea (flower extract), [3]	-	-	X	Protective effects of a flavonoid fraction against gastric lesions; gastric mucus ↑, PGE_2 ↓
Boswellia serrata (extract), [34]	-	-	X	Antiulcer action: increased gastric mucosal resistance, prostaglandin synthesis
Carica candamarcensis (fruit), [20]	-	-	X	Increased mucus content
Citrullus lanatus (juice), [27]	-	-	X	Reduction of gastric lesions; inhibition of gastric acid secretion
Croton cajucara Benth (bark), [16]	-	X	X	PGE_2 ↑; stimulation of gastric mucus secretion
Curcuma longa/*turmeric* (powder), [19, 38]	-	X	-	Anti-inflammatory; antioxidant; antimicrobial; antiplatelet; anticancer; antisecretory; - iNOS ↓
Emblica officinalis (alcoholic extract), [4]	-	-	X	Antisecretory and antiulcer activity; cytoprotective property
Enantia chlorantha (alcoholic bark extract), [23]	-	-	X	Increased mucus production
Eucalyptus citriodora (extract), [9]	-	-	X	Reduction of gastric lesions; increased mucin content; anti-inflammatory activity (reduction of pro-inflammatory markers: IL-1β, TNF-α, 5-LO and COX-2); absence of haemorrhage and necrosis
Gynostemma pentaphyllum (whole plant extract), [29]	-	-	X	Maintenance of gastric mucus production
Lobaria pulmonaria (L) Hoffm (aqueous extract/tea), [35]	-	-	X	Anti-inflammatory and antiulcerogenic effects
Mahonia bealei, [36]	-	-	X	Peptic activity ↑; mucin levels ↑; H^+, K^+, ATP-ase ↓; gastrin levels ↓
Mammea Americana L./ *Guttiferae* (fruit extracts: EtOH, MeOH, DCM), [41]	-	X	-	Reduction of ulcerative lesions and increase of pH by EtOH and DCM extracts; no antiulcer action of MeOH extract
Mikania laevigata Schultz Bip (hydro-alcoholic leaf extract), [7]	-	-	X	Antisecretory and cytoprotective activity
Momordica cymbalaria	-	-	X	Reduction of gastric secretion volume

Phytotherapeutic remedy, bibliographic source	Preclinical study			Main action monitored and demonstrated
	Rabbits/Cats	Mice	Rats	
(unripe fruit), [6]				pH ↑; total acidity and free acidity ↓
Moringa oleifera (fine aqueous leaf extract), [32]	-	-	X	Prevention of ulcer by the modulation of 5-HT secretion through 5-HT_3 receptors in the gastrointestinal tract
Neurolaena lobate (hydro-alcoholic extract of aerial parts), [14]	-	-	X	Alteration of gastric juice parameters: pH ↑ and the amount of gastric juice ↓; increase of prostaglandin synthesis and mucus amount
Ocimum gratissimum (extract), [26]	-	-	X	Mucus amount ↑; gastric acid secretion ↓
Peganum harmala (seeds), [43]	-	-	X	Anti-inflammatory activity; total acidity and free acidity ↓; mucin secretion; inhibition of H^+, K^+, ATP-ase *in vitro*
Portulaca oleracea (aqueous and ethanol extracts) [13]	-	X	-	Reduction of gastric acidity
Rubus idaeus (lyophilized fruit), [1]	-	-	X	Increase of cellular antioxidant enzymes levels; reduction of lipid peroxidation levels
Solanum paniculatum L. (*Jurubeba*) (aqueous extract of flowers, fruit, leaves, roots, stems), [22]	-	X	-	Inhibition of gastric acid secretion by the aqueous root, stem and flower extracts; no alteration of gastric secretion by the aqueous leaf extract; stimulation of gastric acid secretion by the aqueous fruit extract
Stachytarpheta cayennensis (lyophilized aqueous extract of flowers, fruit, whole plant), [21]	-	X	X	Stimulation of intestinal motility by the flower and leaf extracts; no analgesic and anti-inflammatory effect of the whole plant extract
Strychnos potatorum Linn (aqueous seed extract and powder), [31]	-	-	X	Antiulcer, antisecretory and mucoprotective activity
Terminalia chebula (fruit), [24]	-	-	X	Total acidity and free acidity ↓; mucin secretion↑; inhibition of K^+, ATP-ase *in vitro*
Tinospora cordifolia Miers (extract), [28]	-	-	X	Gastroprotective effect: increased levels of PGE_2, anti-inflammatory cytokines and pro-angiogenic factors
Trichopus zeylanicus Gaertn. (alcoholic extract), [33]	-	X	-	Reduction of stress
Usnea longissimi (extract), [5]	-	-	X	LPO↓, SOD ↑, GPx ↑, GSH ↑, CAT ↓, MPx ↓, iNOS ↓, CNOS ↑
Vernonia kotschyana sch. bip. (aqueous extract), [12]	-	-	-	Reduction of the severity of ethanol-induced ulcers
Voacanga Africana (leaf extract), [37]	-	-	X	Cytoprotective, antisecretory and ulcer healing effects
Xylocarpus granatum (fruit), [18]	-	-	X	Inhibition of H^+, K^+, ATP-ase *in vitro*; antiulcer, antisecretory activity

IL-1β – interleukin 1 β, TNF-α – tumour necrosis factor, 5-LO – 5-lipoxygenase, iNOS – inducible nitric oxide synthase; MDA – malondialdehyde; GSH – glutathione; NO – nitric oxide; COX-2 – cyclooxygenase 2; PGE_2 – prostaglandin; LPO – lipid peroxidation; SOD – superoxide dismutase, GPx – glutathione peroxidase, CAT – catalase, MPx – myeloperoxidase, CNOS – constitutive nitric oxide synthase, EtOH – ethanol, MeOH – methanol, DCM – dichloromethane, 5-HT – serotonin, 5-HT3 – serotoninergic receptors

This study was carried out in order to evaluate the state of knowledge on the alternative therapies in gastric secretion. Specifically, medicinal plants, used so far in the treatment of this type of secretion, for which preclinical studies are available, were identified and presented in the table above. Their antiulcerogenic activity was demonstrated by studies on mice, Wistar rats, rabbits and cats. The arguments in favour of the medicinal plants were: increased gastric acid and mucus secretion, prostaglandin synthesis, decrease of MDA, GSH, NO, inhibition of COX-2 activity, increase of pH, reduction of the free and total acidity. A decrease of gastric lesions, an elevation of mucin levels and an inhibition of H^+, K^+, ATP-ase, as well as a modulation of 5-HT secretion through 5-HT_3 receptors in the gastrointestinal tract were also found.

For the preclinical evaluation of medicinal plants, certain extracts (MeOH, EtOH, water/tea) of flowers/ seeds/whole plants/bark/leaves, as well as fresh juices, powders and lyophilized fruit such as black raspberry were used. In some cases, the antisecretory/antiulcer effects of certain substances in the composition of medicinal plants, such as the diterpenoid aparisthman from the *Aparisthmium cordatum* extract [17] and a certain flavonoid fraction obtained from the *Bidens aurea* flower extract [3], were monitored.

In addition to the treatment of gastric secretion, the phytotherapeutic remedies presented in the table are recommended also for other disorders. Thus, in Romania, due to their anti-inflammatory action and

analgesic effect, *Boswellia serrata* tablets are recommended in rheumatoid polyarthritis, chronic degenerative rheumatism, muscle pain, neuralgia, ulcerative colitis and Crohn disease. Some others species are intensively studied in Romania for their antioxidant, antimicrobial, and antiinflammatory properties that would allow further development and use of natural products [39, 40]. Others are used for special zootechnical treatments to decrease cholesterol in broiler chickens - *Berberis lycium* root bark [8].

Over the past years, aside the preclinical studies, also the number of clinical studies on phytotherapeutic preparations has increased and the results of these studies have been disseminated in scientific meetings (e.g. the Congress of the Romanian Association of Phytotherapists in 2015) or published in specialized journals. Some of these clinical studies assessed the efficacy of indigenous alfalfa in oncology, of *Rumex carbo* in Wilson's syndrome, or the metabolic efficacy and adherence to phytotherapy in a group of patients with early type 2 diabetes mellitus. The phyto-therapeutic approach of genital inflammatory disorders, of non-alcoholic steatohepatitis, of depression and other mental disorders, and the gemmotherapy in skin diseases were also assessed in different clinical studies.

These phytotherapeutic preparations are available in several member states of the European Union. For the protection of public health, the collection, processing and storage of phytotherapeutic intermediary and end products, as well as their distribution and marketing, should take place under the best hygiene and quality conditions, with the observance of the best practice guidance. Regardless of the type of phytotherapeutic products – "conventional use"/well-established use or "stand alone" drugs, manufacturers have the legal obligation to demonstrate at any time the quality of the plant preparation. Also, alike for allopathic drugs, the safety of the phytotherapeutic products should be permanently monitored and assessed; for this, it is important that adverse events and reactions, and especially serious adverse reactions are reported to regulatory agencies when suspected.

Phytotherapeutic products represent a valuable alternative therapy for patients who do not respond to conventional drug therapy or for those with mild/ moderate gastric hypersecretion or without other more severe associated gastrointestinal disorders. However, phytopreparations have both advantages and disadvantages compared to allopathic drugs. Some of the advantages of these products consist of the fact that they can be better tolerated than conventional drugs, do not have so many drug interactions, are frequently less expensive, and many of them can be stored under the same conditions as allopathic drugs. Moreover, most phytotherapeutic products are available in various forms, such as simple or compound tinctures, fatty oils and compound classic syrups, creams and gels, soft capsules, tablets, soluble preparations, ovules and suppositories or teas, all these natural remedies being readily available to patients. The main disadvantage of phyto-preparations probably is that this type of products is regarded with scepticism by certain doctors or users. This might be probably due to the lack of extensive clinical evaluations to demonstrate efficacy and safety, compared to allopathic drugs. Another disadvantage is the lack of standardised and reproducible products.

Conclusions

The present review outlines the significant gastric antisecretory effects of medicinal plants, demonstrated in numerous preclinical studies. This provides scientific validation for their use in various forms (extracts, tinctures, powders, juices etc.). While preclinical research on medicinal plants in gastric secretion is extensive, we consider that appropriate clinical studies of these phytotherapeutic remedies should be further developed to demonstrate efficacy.

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