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Biological relevance of diverse natural products from Gastomel product: A general view on different classes

Natural products (phenolic substances, terpenoids, fatty acids etc.) have played a significant role in human disease therapy and prevention (1). Aromatic plants had been used since ancient times for their preservative and medicinal properties, and to impart aroma and flavor to food. Modulation of the immune system, for example, may offer novel approaches in the treatment of a variety of diseases. One strategy in the modulation and involvement of the immune system may be through the use of herbal medicines. A class of herbal medicines, known as immunomodulators, alters the activity of immune function through the dynamic regulation of informational molecules such as cytokines (2). This may offer an explanation of the effects of herbs on the immune system and other tissues. Herbal medicines contain an abundance of phenolic substances, terpenoids and other natural antioxidants that have been also associated with regulation of activity of the digestive system and serving as a natural antibiotic against the *Helicobacter pyloris* bacteria, which causes ulcers and infections in the digestive system. They are now used by up to 50% of the Western population, in a substantial minority of instances for the treatment or prevention of digestive disorders (3).

For this informal review, we will survey the primary literature on diverse classes of naturally occurring compounds that were found in GASTOMEL product and we will follow their

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effects on the gastrointestinal tract, stomach and digestive system, taking special care to analyze the compounds of the plants that were used in the production of GASTOMEL and laboratory analytical results obtained from National Residue Control Laboratory.

Methodology

Search Strategy

The databases PubMed, SciFinder, ISI web of knowledge, and general scientific sources in the internet were searched for appropriate studies. Titles were screened for all hits to the terms that include the diverse classes of compounds with or w/o the requested activity and in comparison with the information obtained for the relevant main plants that were used in the production of Gastomel product (table 1).

Main classes	**Biological relevance**	**Main plants that were used for the feeding of the bees**
Terpenoids; Flavenoids; Fatty acids	Regulator of digestive system Antiulcerative Natural antibiotic against *Helicobacter pyloris*	*Laurus nobilis* *Salvia officinalis* *Angelica atropurpurea* *Hydrangea arborescens* *Opuntia ficus-Indica* *Medicago sativa*

Table 1

1. The group of terpenoids:

The nomenclature of terpenoids depends on the number of isoprene structures and their carbon atoms in the molecule (table 2). Turpentine contains the "resin acids" and some hydrocarbons, which were originally referred to as terpenes. Traditionally, all natural compounds built up from isoprene subunits and for the most part originating from plants are denoted as terpenes (4). Terpenes are widespread in nature, mainly in plants as constituents of essential oils. The main terpenes that were detected at Gastomel product are: 1-8 cineole (eucalyptol), α-terpinene, thujone, citronella, Linalool, Eremophilene, caryophyllene,

Caryophyllenol, Verdiflorol, Vulgarol B, Spathulenol, beta-himachalene, Longifolenaldehyde, Benzyl cinnamate, beta- Selinene, Junipene, Linalol oxid, Isolimonene, beta -Eudesmol

Terpenoid item	C atoms	Isoprene structures
Monoterpene	10	2
Sesquiterpene	15	3
Diterpene	20	4
Triterpene	30	6
Tetraterpene	40	8
Polyterpene	>40	>8

Table 2: Nomenclature of terpenoids

Monoterpenes and Sesquiterpenes

Monoterpenes and Sesquiterpenes are non-nutrient dietary components and are best known as constituents of the essential oils. In general, sesquiterpenes are less volatile than monoterpenes. Monoterpenes and sesquiterpenes were investigated especially concerning their chemotherapeutic, digestive and antiulcerative activities (5, 6).

Recently groups of monoterpenes and sesquiterpenes were isolated from *Laurus nobilis* (Bay laurel) a plant with well known reducing of gastric fluid secretion and work against digestive disorders as flatulent colic (7); also from other plants found in Gastomel product. Combinations of dietary chemopreventive agents can sometimes result in significant activities at concentrations where any single agent is inactive. Many of the phytochemicals are reported to act synergistically. The molecular mechanism underlying such synergistic effects is still incomplete, but it seems that different combinations of complementary modes of actions are involved (8).

Digestive Activity of Monoterpenes and Sesquiterpenes

Recently groups of monoterpenes and sesquiterpene were isolated from *Laurus nobilis, Salvia officinalis, Angelica atropurpurea, Hydrangea arborescens, Opuntia ficus-indica* and *Medicago sativa.*

Recent studies reveal that leaves and essential oil of *Laurus nobilis* obtained from the leaves increase gastric fluid secretion and work against digestive disorders as flatulent colic (7).

1,8 cineol from *Laurus nobilis* has a gastroprotective effect on ethanol-induced gastric mucosal damage in rats. When 1,8-cineole was tested on pylorus-ligated rats, the smaller dose (50 mg/kg) produced an increase in gastric mucus content, gastric secretory volume, and total acidity and higher doses (100 and 200 mg/kg) resulted in significant inhibition of gastric secretory volume and total acidity, suggesting its modulatory influence on gastric secretion. The effect of 1,8-cineole on ethanol-induced gastric injury, however, seems to be independent of its effect on gastric secretion and gastric mucus since gastroprotection was observed at almost all doses employed. Cineole also significantly reduced the myeloperoxidase activity, and caused repletion of glutathione. These results confirm the anti-inflammatory action of 1,8-cineole and suggest its potential value as a dietary flavoring agent in the prevention of gastrointestinal inflammation and ulceration (9, 10).

Several researchers have noted the potential *Salvia* (Sage) has in helping the medical community find cures to serious medical conditions. Sage has a very long history of effective medicinal use and is an important domestic herbal remedy for disorders of the digestive system. It is highly serviceable as a stimulant tonic in debility of the stomach and nervous system and weakness of digestion generally. Its antiseptic qualities make it an effective gargle for the mouth where it can heal sore throats, ulcers etc. The leaves applied to an aching tooth will often relieve the pain (11).

Decoction of *Salvia* leaves being used against digestive disorders. It settles an upset stomach, relieves gas and bloating after meals. Additionally it calms inflammation of the digestive tract, soothes irritated membranes, relieves excess sweating, night sweats and dries up congested mucus (12, 13).

For centuries, many species of *Angelica* genus, including *A. atropupurea* have been used traditionally as anti-inflammatory, diuretic, expectorant and diaphoretic, and remedy for colds, flu, influenza, hepatitis, arthritis, indigestion, coughs, chronic bronchitis, pleurisy, typhoid, headaches, wind, fever, colic, travel sickness, rheumatism, bacterial and fungal infections and diseases of the urinary organs. It is a remedy for colic, gas, sour stomach and heartburn. It improves circulation, warms the body and relieves spasms of the stomach and bowels. Active principles isolated from these plants mainly include various types of coumarins, acetylenic compounds, chalcones, sesquiterpenes and polysaccharides (14, 15). These compunds have an warming circulatory tonic effect that relieves gas, bloating and colic. Also it has anti-inflammatory and anti spasmodic effects (13).

The Hydrangea genus appears to contain few of the less usual flavonoid compounds, but the coumarins umbelliferone and hydrangetin (8-O-methyldaphnetin) were present in all the species (16).

The nutritional properties of the fresh stems (cladodes) of the prickly pear (*Opuntia ficus indica*) have long been known, and prickly pear is used also in traditional medicine for its hypoglycemic and hypolipidemic actions. (17). Mexicans have used *Opuntia* leaves and fruits for their medicinal benefits, such as for treating arteriosclerosis, diabetes, gastritis, and hyperglycemia. The antioxidant activity of *Opuntia ficus* is reported to correspond to well-known antioxidants, such as catalase, R-tocopherol, and ascorbic acid in a cell-free reactive oxygen species generating system (18) Furthermore, Lee et al. postulated an antiulcerogenic effect of the cladode or fruit powder from *O. ficusindica* var. *saboten* Makino. Stomach lesions triggered by hydrochloric acid/ethanol or hydrochloric acid/acetylsalicylic acid were reduced, but no anti-inflammatory effect could be proven. The secretion rate of both gastric juice as well as the pH value remained constant (19, 20). Galati et al. confirmed these results. However, the protective effect was ascribed to the cladodes' hydrocolloid acting as a buffer, spreading out on the gastric mucosa and increasing mucus production by enhancing the number of secretory cells (21).

Extracts or tinctures of *Medicago sativa* are used in both human and veterinary medicine for the treatment of a variety of disorders. Traditionally, alfalfa (*Medicago sativa*) has been used for the treatment of sore throat, anemia, stomach ulcers (22). One of its most common uses in Chinese medicine is in the treatment of ulcers. It is also used to strengthen digestion and stimulate appetite. Herbalists have long used alfalfa to treat ulcers, with good results. The bioflavonoids found in alfalfa build capillary strength and reduce inflammation of the stomach lining, while alfalfa's vitamin A helps to maintain the stomach's health. The herb's enzymes aid in food assimilation (23).

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