SENNOS

Journal of Drug Delivery and Biotherapeutics

Journal homepage: https://sennosbiotech.com/JDDB/1

Review Article

Exploring the Efficacy of Herbal Medicines in Alleviating Constipation: A Comprehensive Review

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ARTICLEINFO

ABSTRACT

Constipation is a prevalent global health concern, particularly impacting women and exerting a substantial toll on health-related quality of life. Originating from diverse factors, including lifestyle choices (functional constipation), diseases, and medications, it manifests with symptoms such as abdominal pain, distension, anorexia, and nausea. While conventional recommendations advocate increased fluid intake, physical activity, fiber-rich diets, and nutritional supplements for relief, their efficacy remains uncertain.

This comprehensive review delves into the multifaceted landscape of constipation treatment, exploring not only conventional pharmaceutical interventions but also the potential of herbal drugs. Botanical laxatives like senna, cascara, frangula, aloe, and rhubarb take center stage, scrutinizing their utilization and efficacy in managing constipation. The review critically assesses the value of these herbal interventions and underscores their role in preventing and treating this pervasive disorder. The review sheds light on recent investigations that have advanced our understanding of herbal drugs in constipation treatment. The exploration encompasses emerging perspectives.

Keywords: Herbs; Constipation; Laxatives; Herbal Drugs; fiber-rich diets

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Received date: 10-Mar-2024 Revised date: 25-Mar-2024, Accepted date: 15-Apr-2024

Crossref DOI: https://doi.org/10.61920/jddb.v1i01.19

1. Introduction

Constipation is a disorder of the gastrointestinal tract, which can result in infrequent stools, difficult stool passage with pain and stiffness. Constipation may cause closure of the intestine, which may even require surgery[1]. It is worth noting that there is currently no ideal definition for constipation; thus, history and physical examination can be considered the main initial approaches. Many definitions are described by using self-reported constipation and the formal criteria[2]. Many definitions of constipation are related to scientific considerations such as secondary causes (medications), neurological, or systemic diseases. However, it is considered primary or idiopathic. Pathogenesis is multifactorial with focusing on genetic predisposition, socioeconomic status, low fiber consumption, lack of adequate fluid intake, lack of mobility, *disturbance* in the *hormone balance*, side effects of medications, or anatomy of the body, etc[3]. Constipation is a common gastrointestinal problem, which causes many expenses for the community with an estimated prevalence of 1% to 80%, worldwide, where the condition is characterized by a wide geographical variation. Constipation is a complicated condition among older individuals, which is characterized by difficult stool passage[4]. Different types of therapies used to cure constipation including Lubiprostone, Linaclotide, Prucalopride, Colchicine, Alvimopan also Surgical interventions may be used as an option if medical treatment was failed in constipated patients and mechanical emptying of the colon may be recommended in patients with slow bowel movements using an enema program[5]. Colectomy with ileorectal anastomosis has been introduced to be the treatment option for constipation but all these treatments may produce adverse effects or some time it may be expensive. Therefore, herbal medicine is a good choice for constipation treatment which produces fewer toxic effects and helps to cure constipation[6]. Herbal plants in constipation treatment include senna, rhubarb, psyllium, Prunus persica (Rosaceae), Cyamopsis tetragonolobus (Leguminosae), Citrus sinensis (Rutaceae), Planta goovata (Plantaginaceae), Rheum Emodi (Polygonaceae), Cassia auriculata (Caesalpiniaceae), Ricinus communis (Euphorbiaceae), Croton tiglium (Euphorbiaceae), Aloe Barbadensis (Liliaceae), Mareya micrantha (Euphorbiaceae), Euphorbia thymifolia (Euphorbiaceae), Cascara sagrada (Rhamnaceae), Cassia Angustifolia (Fabaceae) which produce laxative activity with fewer adverse effect s[7]. This review focuses on herbs used in constipation and throws light on a recently developed investigation on herbal drugs for constipation. Before delving into the drug used in constipation treatment common causes of constipation are described shortly in the subsequent section.

2. Common Causes of Constipation

2.1. Disease induced constipation

Diabetes mellitus may lower the peristaltic movements and secretion of gastrointestinal glands same as in hypothyroidism. Uraemia can produce mucosal abnormalities which may lead to ulceration while Amyloidosis can decrease the secretion of endocrine cells that secrete hormones like serotonin and also alter the motility of the intestine. Neuropathy and spinal cord injury impairs sensory and motor function and slow the transit time[8].

2.2. Drug-induced constipation

Medications are the important secondary cause of constipation and especially those drugs which affect the central nervous system, nerve conduction, and smooth muscle function. Such type of constipation can easily be measurable by calculating the colonic

transit time, anorectal manometry, defecography, or balloon expulsion test. The NSAIDs are used to relieve pain but also reduce the mucous and bicarbonate secretion while antihistaminic inhibits gastric acid secretion. Anticholinergics drugs like carbamazepine and diuretics may inhibit sodium channels while sympathomimetics like ephedrine relaxes the smooth muscles of the intestine and muscle relaxants, antimotility drugs like diphenoxylate reduce peristalsis and ultimately constipation[2].

2.3. Diet

A fiber-rich diet accelerates transit time, softens stool, and increases stool weight, but a diet that is poor in fiber can induce constipation. However, the consumption of dietary fiber is no different between constipated and non-constipated subjects. Increasing dietary fiber improves symptoms in patients with normal colonic transit and anorectal function, but not in constipated patients with delayed colonic transit and defecation disorders. The latter is characterized by low stool weight and prolonged transit times regardless of the amount of fiber in their diet, which suggests that increasing their fiber intake does not normalize colonic transit and can even worsen their symptoms as a result of the gas produced by fiber metabolism.

2.4. Colonic motility and absorption

Delayed colonic transit is associated with small and hard stools that are difficult to evacuate. It has been found that fecal consistency and water content significantly correlate with colonic transit time, which suggests that prolonged colonic transit favors the time-dependent process of water absorption. Moreover, changes in colonic transit affect bacterial mass, and this may also influence colonic absorption and secretion. Delayed colonic transit may be due to impaired colonic motor activity, but may also be secondary to voluntary stool retention, defecation disorders, or an inadequate caloric intake. Studies of colectomy samples taken from patients with delayed colonic transit suggest that impaired motility might be caused by abnormalities in interstitial cells of Canal or the overexpression of progesterone receptors in colonic circular muscle cells. However, the normalization of delayed transit after behavioural treatment in such patients, and changes in the male/female incidence ratio of constipation in patients aged > 60 years, suggest that structural abnormalities should not be considered an irreversible cause of impaired colonic motility[9].

2.5. Behavioural factors

Withholding behaviour after experiencing a difficult and painful bowel movement is known to induce functional constipation in children and leads to stool retention, rectal distension, and overflow faecal incontinence. The problem may persist into young adulthood and returns to being a major cause of constipation in elderly hospitalized patients whose persistent disregard of the call to stool may lead to faecal impaction. Table.1 summarises the most prevalent causes of constipation.

Table.1: Common causes of constipation [10]**.**

Cause	Comment
Diet	A diet low in both soluble and insoluble fiber. Experts recommend a daily intake of 20 to 35 g of fiber.
Inadequate liquids	A daily intake of 1.5–2 mL of fluids makes the stool softer and easier to pass throughout the large intestine.
Inactivity	The lack of physical activity leads to constipation.
Live change	Constipation is a common problem during pregnancy, mainly in the last 6 months, as a result of hormonal change and pressure from the uterus on the intestine
Changes in routine	Traveling, stress and overwork can often lead to constipation

3. BOTANICAL LAXATIVES FOR CONSTIPATION TREATMENT

Anthraquinone drugs (e.g., senna, cascara, frangula, aloe, and rhubarb) induce and facilitate defecation by rescuing altered motility patterns and increasing colonic fluid volume. Anthraquinones are glycoside derivatives of anthracene. The glycosides behave like pro-drugs, liberating the aglycone that acts as the effective laxative[11]. The metabolism of glycosides takes place in the colon on behalf of bacterial glycosidases: the products obtained are poorly absorbed and act by evoking secretion and motility changes in the colon. The effect on secretion and motility is, at least in part, due to the release of prostaglandins and other autacoids. The mechanism of action of anthraquinones aglycones also includes the inhibition of colonic NaCl absorption and the stimulation of Cl secretion, explained by the inhibition of the (Na+, K+)-adenosine triphosphatase[12]. The laxative action of anthraquinones occurs 6–12 h after oral ingestion. Colic pain associated with the use of large doses of crude anthraquinone drugs is prevented by the use of lower doses or purified glycosides. Anthraquinone drugs are currently recommended for short-term treatment (1–2 weeks) of atonic constipation, some cases of acute constipation, and before endoscopy of the lower gastrointestinal tract; they are not advisable for spastic constipation[13]. Anthraquinones in combination with fiber are also effective and well-tolerated for the treatment of chronic constipation in elderly patients. The side effects of anthraquinones include discoloration of the urine, reversible melanosis of the colon, and haemorrhoid congestion. No changes in serum electrolyte levels were found with recommended doses of anthraquinones [14]. Contrary to what was first believed, the treatment of constipation with anthraquinone drugs in lactating mothers does not carry a risk of producing a laxative effect in the infant. Moreover, the treatment with senna does not induce any increased risk during pregnancy or for the fetus. Anthraquinone drugs are ingredients of proprietary products and several over-the-counter laxatives [15].

Senna

Among all the anthracoid laxatives, senna is certainly the most used one. Senna consists of the dried leaves and pods of Cassia Acutifolia (Cassia senna) Delile, known in commerce as Alexandria senna, or of Cassia Angustifolia Vahl, known as Tinnevelly senna. Cassia species are native of

Egypt, the Middle East area (Somalia, the Arabian Peninsula), and India; these shrubs grow up to 20–60 cm and are characterized by paripinnate compound leaves, arranged in clusters of four to seven small leaves opposite each other with an elongated painted form[16]. The fruits are pod-like, blackish, elongated, flat, and kidney-shaped. The laxative effect of leaves is greater than that of fruit. Dianthrone glycosides (1.5–3% in the leaf; 2–5% in the fruit), namely, sennosides A and B, together with other anthraquinone derivatives (aloe-emodin and rhein), are responsible for the laxative action of senna. Sennosides A and B can be regarded as pro-drugs; they reach the large intestine without changing and are hydrolyzed by the bacterial flora to generate the main active metabolites rhein and rhein-anthrone[17]. These metabolites act upon both the secretion and motility to cause laxation, and these actions are largely independent of one another. Although senna is not as mild in its action as cascara and frangula, it is more widely used because it is considerably cheaper. Senna is taken in the form of tea (prepared from 0.5 to 2 g of leaves or fruit), fluid extract (2 mL), or syrup (8 mL). Such preparations usually produce a single bowel evacuation within 6 h. However, some users prefer the beverage prepared by soaking senna in cold water for 10–12 h and then straining. This preparation is more active than hot tea because it contains more sennosides and less resinous material. Crystalline senna glycosides (sennosides A and B) are also commercially available (usual dose 12/36 mg); they are more stable, more reliable, and safer than the preparations from crude senna[18].

Cascara

Like senna, cascara also contains anthraquinone glycosides (Cascarosides A, B, C, and D) with other anthraquinone glycosides in minor amounts. The drug consists of the dried bark of the trunk or branches of the Rhamnus Purshiana, a shrub that grows along the Pacific coast of North America[19]. The bark needs to be collected at least 1 year before use, to allow the reduced emodin-type glycosides to be oxidized to monomeric forms that exhibit a milder cathartic activity. Cascara must contain not less than 7% of total hydroxy anthracene derivatives calculated as Cascarosides A on a dried basis. Because of its mild action, cascara produces weak side effects (griping). Cascara is used in the form of extract, fluid extract, aromatic fluid extract (5 mL usually causes laxation), and powder (1 g in capsule form). Cascara tea is not popular because of its extremely bitter taste. Purified anthranol glycosides (casanthranol) from cascara are also available (30 mg). The laxative action occurs after about 8–12 h. Cascara is an ingredient of several over-the-counter laxatives[20].

Frangula

Frangula consists of the bark of Rhamnus frangula, a shrub that grows in Europe and western Asia. Like cascara, frangula should be collected 1 year before use. Its laxative effect is due to the presence of anthraquinone derivatives, particularly, glucofrangulin A and B: the drug must contain not less than 6% of total hydroxy anthracene derivatives calculated as glucofrangulin A on a dried base. Frangula is comparable with cascara in its relatively gentle laxative action. It is used in the form of fluid extract, but it is also possible to consume the powdered bark (1 g) in capsule form. The laxative action occurs after about 10–12 h[21].

Aloe

The drug consists of the solid residue obtained by evaporating the latex that drains from the transversally cut leaves of several species of Aloe (Aloe Barbadensis, Aloe ferox, etc.). The anthraquinone glycosides aloins A and B account for

the laxative action of aloe. In addition to aloins (10–30%), aloe contains volatile oil and large amounts of a resinous material (16–63%). Taken in doses of 0.25 g, aloe causes its laxative action after 6–12 h with loose bowel movements accompanied by abdominal pain. Among the anthraquinones, aloe possesses the most potent action: it is less employed now because it tends to cause griping, persisting over several days [22].

Rhubarb

Rhubarb consists of the dried rhizome of Rheum palmatum L., Rheum officinale L., or of related species. The drug is of various forms (cylindrical, oval, and round) and size (5–15 cm in length and 4–10 cm in diameter). Rhubarb contains sennosides A–F with laxative properties, a considerable quantity of tannin. The drug, like aloe, is much more potent than cascara, frangula, or senna. Its use almost always causes intestinal griping or colic. However, a laxative action without abdominal pain is caused by a dose of 0.5–2 g. The most used preparations are tinctures, infusions, and fluid extract [23].

4.Recently Developed Investigation on Herbal Drugs For Constipation

4.1 Investigation on Senna

Senna is one of the most frequently employed botanical laxative remedies and a well-recognized drug used in the allopathic and Ayurvedic systems of medicine. **(*Jalwal et.al*)** formulate enteric-coated tablets of senna extract and ajowan oil was successfully formulated by using cellulose acetate phthalate coating materials and could be completely averted initial loss of sennosides in the stomach for the treatment of constipation. The results of this study indicate that enteric-coated tablets using 12% CAP are suitable for the senna drug which is mainly active in the lower Gastrointestinal tract [24].

(Feudenter et.al) studied the comparative effect of senna in pediatric oncology patients who receive opioids. The author performed a retrospective cohort study of hospitalized pediatric oncology patients less than 21 years of age in 78 children's and adult hospitals between 2006 and 2011 who were started on seven consecutive days or more of opioid therapy and were started on an oral bowel medication within the first two days of opioid therapy. Initiating senna therapy within two days of starting the prolonged opioid course, compared with initiating another oral bowel medication, was significantly associated with a lower hazard during the ensuing five days for receipt of an enema (hazard ratio [HR], 0.31; 95% CI, 0.11–0.91) or undergoing abdominal radiographic imaging (HR, 0.74; 95% CI, 0.55–0.98), was marginally associated with a lower hazard of oral bowel medicine escalation (HR, 0.78; 95% CI, 0.59–1.03), and overall was significantly associated with a lower hazard of the composite endpoint of problematic constipation (HR, 0.70; 95% CI, 0.56–0.88). The study concluded that Initiating senna therapy, compared with other oral bowel medications, diminishes the subsequent risk of surrogate markers of problematic constipation in this population [25].

4.2 Investigation on *Amorphophallus paeoniifolius* (Dennst.)

Amorphophallus paeoniifolius (Dennst.) is an Ayurvedic medicinal plant useful for the treatment of gastrointestinal diseases viz. hemorrhoids, vomiting, anorexia, dyspepsia, flatulence, constipation. **(Dey et.al)** the revealed laxative effect of this plant in the constipation-induced rat. The author extracts the tuber of the plant with methanol and identified two actives constitute betulinic acid and β-sitosterol. The activity of compounds tested by administering loperamide in a rat model to induce constipation. The results indicated that tuber

extracts and their active constituents showed laxative effects and relieving constipation. From the study, it is concluded that the tuber of *A. paeoniifolius* exhibited a beneficial effect in functional constipation possibly through its laxative action[26].

4.3 Investigation on Rhubarb

Rhubarb contains important active ingredients such as chrysophanol, aloe-emodin, rhein, emodin, and physcion and has many pharmacological activities including purgative, anti-inflammatory, anti-cancer, anti-angiogenesis. **(Gao et.al)** reveled rhubarb extract relieves constipation by stimulating mucus production in colon and intestinal flora. Rhubarb promotes the secretion of colonic mucus by recruiting mast cells and enhancing the content of histamine and Ach in the mice colon. In the process, Rhubarb causes up-regulation of Bip and CHOP mRNA expression and down-regulation of Xbp1 and Xbp1s mRNA expression that induces ER stress of colonic epithelium associated with changes in the intestinal flora diversity and short-chain fatty acids content. From Study concluded that Rhubarb could relieve constipation by promoting the secretion of colonic mucus *via* mast cells activation and improving the intestinal microenvironment[27].

4.4. Investigation on Mallaw

Mallaw (*Malva sylvestris* L.) is a medicinal plant that is traditionally being used as an antiulcer, laxative, and anti-haemorrhoid, besides its culinary use as a food in Tunisian cuisine. **(Jabri et.al)** evaluate the protective effect of *Malva sylvestris* aqueous extract (MSAE) on constipation-induced by loperamide in male *Wistar* rats. Constipation is induced in the rat by administrating loperamide. The MSAE (100, 200, and 400 mg/kg; *b.w*, *p.o*.), significantly reduced loperamide-induced constipation in a dose-dependent manner. The author concluded that MSAE had a potent effect against Loperamide-induced constipation through in part to an increase of gastrointestinal motility, stimulation of water intestinal secretion as well as its antioxidant properties.

5. CONCLUSION

Constipation is the most common digestive disorder. It is defined as abnormal bowel movements and feces that are small, dry, and difficult to pass. This review article presents important medicinal plants for the treatment and prevention of constipation. These plants can be used for the preparation of new drugs; their active ingredients may also be used in the treatment of constipation. In future studies, it is better to focus on the classification of herbal laxatives, based on their mechanisms for treating constipation.

Acknowledgment

We would like to thank the Department of Pharmaceutics, Department of pharmaceutics, Dr D Y Patil Institute of pharmaceutical sciences and Research Pimpri, Pune forgives guidance and support for conducting a research study.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Authorship Contribution Statement

Sunil Kanadje: Supervision, Validation, Methodology, Investigation, Writing – original

draft, **Jitendra Hiwarkar:** Conceptualization, Administration, Funding, Data Curation.

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