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Review Article

Anti-Spasmodic Activity of Different Herbal Plants

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ABSTRACT

Many medicinal plants have been employed to address various diseases and disorders, particularly gastrointestinal (GI) conditions, which are prevalent among children and adolescents. These GI diseases are not only some of the most common health complaints in this demographic but also often present overlapping clinical symptoms that complicate diagnosis and treatment. As a result, effective management requires a nuanced understanding of these disorders' physiological and psychological aspects. In therapeutic interventions, drugs with antispasmodic effects are frequently utilized to alleviate symptoms such as contractions and cramping of smooth muscles, which are common in gastrointestinal diseases and other critical medical situations. Moreover, in alternative systems of medicine, antispasmodic herbs have been integral to the treatment of GI ailments, reflecting a deep-rooted tradition of utilizing natural remedies for health maintenance. The enduring use of these medicinal plants and their herbal products across generations can be attributed to their diverse nutritional and therapeutic benefits. Their effectiveness may be linked to biologically active chemical constituents contributing to their healing properties. This review aims to explore the medicinal potential of plants known for their antispasmodic activities, delving into their proposed mechanisms of action and highlighting the importance of further research in this area. A comprehensive literature search was conducted using several databases, including Google Scholar, Scopus, and PubMed, to gather relevant studies and insights on plants with antispasmodic properties. This study provides a comprehensive and quantified overview of various medicinal plants known for their antispasmodic properties like Zingiber officinale, Foeniculum vulgare, Psidium guajava, and Lavandula angustifolia.

INTRODUCTION

Plants are the main natural source of a large number of bioactive compounds. During time

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immemorial, several diseases have been cured using various plant preparations in folk medicine. and, now, cosmetic, pharmaceutical, and nutraceutical industries are giving greater attention to plant preparations and pure phytochemicals. The plant preparation market will reach up to about USD 86.74 billion by 2022, and pharmaceutical is identified as the largest market share followed by the nutraceutical industry with the use of plant preparations in cosmetics, beverages, food, and medicine mainly by the leaves. The largest accumulators of bioactive compounds, such as secondary metabolites, comprise all organs of the plant. Recently, several articles reported phytochemical profiles as well as the biological activities of leaf extracts from various crops cultivated on farms. Thus, although the leaves of plants are considered agricultural wastes, they constitute an excellent source of high-value Nutra-pharmaceutical compounds. Gastrointestinal disorders are among the most frequently reported health issues in children across the globe, impacting their overall well-being and daily functioning. These disorders encompass a wide array of conditions, including functional abdominal pain, ulcerative colitis, irritable bowel syndrome (IBS), infantile colic, constipation, gastroenteritis, and various acute gastrointestinal disorders. The prevalence of these conditions can lead to significant disruptions in a child's life, affecting their physical health, emotional stability, and social interactions. The implications of gastrointestinal disorders extend beyond physical symptoms. Children suffering from these conditions often experience decreased quality of life, which can manifest as increased anxiety and depression. For instance, chronic abdominal pain can interfere with school attendance, playtime, and family activities, leading to feelings of isolation and frustration. The hallmark of many gastrointestinal disorders is recurrent or chronic abdominal pain. In the case of IBS, this pain may be accompanied by notable changes in bowel habits, such as diarrhea, constipation, or alternating episodes of both. Relief from discomfort is sometimes experienced following defecation, highlighting the complex interplay between bowel function and abdominal pain. IBS is particularly multifaceted, often characterized by abnormalities in intestinal motility. Children with IBS may exhibit symptoms ranging from abdominal cramps and bloating to diarrhea or constipation, which can further complicate their emotional and psychological well-being. For instance, diarrhea is typically associated with loose, watery stools, which can be distressing and embarrassing for children, impacting their willingness to engage in social activities or attend school. Antispasmodic medications are commonly employed to reduce excessive smooth muscle contractions, leading to gastrointestinal cramps, bronchial spasms, and discomfort in the genitourinary tract. A variety of synthetic antispasmodic agents have been approved by regulatory authorities worldwide, including anticholinergic drugs like butylscopolamine, direct smooth muscle relaxants such as papaverine, calcium antagonists like pinaverium, and opioid receptor modulators such as trimebutine. Addressing these disorders requires a comprehensive approach that not only targets the physical symptoms but also considers the emotional and psychological ramifications. Early intervention, dietary modifications, and psychological support can play crucial roles in managing these conditions and improving the quality of life for affected children. Antispasmodics represent a diverse category of medications that primarily target the neurotransmitter acetylcholine. Common examples include hyoscyamine and dicyclomine, which are frequently used in clinical settings to manage various gastrointestinal disorders, including irritable bowel syndrome (IBS) in

adults. However, research on the effectiveness of antispasmodics for functional abdominal pain disorders (FAPD) in children is limited, with existing studies generally yielding suboptimal results. Moreover, the use of antispasmodics in pediatric populations raises concerns about potential anticholinergic side effects, which may include dry mouth, blurred vision, reduced sweating, headaches, dizziness, weakness, sleep disturbances, nausea, vomiting, constipation, and bloating. Given these risks, it is essential to conduct further research to assess the safety and efficacy of antispasmodic treatments in children with FAPD before making clinical recommendations. Ayurveda, the ancient Indian medicine system, emphasizes using natural remedies derived from plants to promote health and well-being. It highlights a range of botanical substances that can effectively alleviate gastrointestinal disorders, such as indigestion, bloating, and constipation. These plant-based treatments are valued for their efficacy and gentle nature, as they typically do not produce the adverse effects commonly associated with synthetic medications. They identify numerous plants that effectively address various gastrointestinal issues without causing side effects such as *Lepidium sativum* (garden cress), *Allium cepa* (onion), *Zingiber officinale* (Ginger), *Foeniculum vulgare* (Fennel), *Lavandula angustifolia mill* (lavender)

Methodology:

Chick ileum and Guinea pig ileum:

Fresh ileum was collected from the slaughterhouse. It was kept at room temperature with adequate aeration in freshly prepared Tyrode solution. The segment of 2 cm was mounted in a 20 ml tissue organ bath. The tissue was allowed to equilibrate for 30 minutes, during which the bathing solution was changed every 10 minutes. The contact time of 60 seconds and baseline of 30 seconds time cycle were opted for proper recording. The dose-response curve of acetylcholine was first recorded on the kymograph. The cumulative concentration-effect curves were recorded on a kymograph for acetylcholine in the absence and presence of ethanolic extract of herbal drugs on the kymograph by using Sherrington's recording drum. The same procedure was carried out for the effect curve of acetylcholine in the presence of the standard drug. The percentage inhibition of extract and standard drug was calculated and the graph was plotted by taking log dose versus height of the response curve.

Antispasmodic herbal plants:

Lepidium sativum

The crude extract of Lepidium sativum (abbreviated as Ls.Cr), commonly known as garden cress and a member of the Brassicaceae family, has demonstrated significant antidiarrheal and antispasmodic effects across various animal models. This plant's therapeutic potential, particularly for gastrointestinal ailments, is supported by both in-vivo and in-vitro studies, which reveal species-specific mechanisms that underlie its pharmacological action.

In mouse models, Ls.Cr has shown an ability to effectively inhibit diarrhea induced by castor oil, a common inducer of gastrointestinal distress, at doses of 300 and 1000 mg/kg. Notably, the dose needed to produce this effect in mice is three times higher than the dose required in rats, indicating variability in sensitivity among species. This antidiarrheal activity points to the potential of L. sativum for treating diarrhea through mechanisms that may involve altering intestinal motility or fluid secretion. In isolated tissue studies, Ls.Cr was tested on the ileum and jejunum of rats, where it completely inhibited contractions induced by the muscarinic agonist carbachol (CCh) as well as contractions triggered by potassium at both moderate (25 mM) and high (80 mM) concentrations. This suggests that Ls.Cr exerts a

potent antispasmodic effect, likely through inhibition of calcium influx, as potassium-induced contractions often rely on calcium-dependent mechanisms. In guinea pig tissues, however, Ls.Cr exhibited selective action, fully blocking only the contractions induced by CCh, highlighting a species-specific response to the extract. In rabbit tissue experiments, Ls.Cr demonstrated complete inhibition of both CCh-induced and low potassium (K+)-induced contractions, which were sensitive to potassium channel blockers. This suggests that, in rabbits, Ls.Cr may exert its effects partially by activating potassium channels, leading to smooth muscle relaxation. Additionally, pretreatment with Ls.Cr in guinea pig and rat tissues caused a rightward shift in CCh-induced contraction curves, similar to the action of dicyclomine, a known anticholinergic agent, indicating that Ls.Cr might block muscarinic receptors, reducing smooth muscle contraction. Conversely, in both rabbit and rat tissues, Ls.Cr caused a leftward shift in isoprenaline-induced relaxation curves, mimicking the action of papaverine, a phosphodiesterase inhibitor and smooth muscle relaxant. This suggests that Ls.Cr might also inhibit phosphodiesterase enzymes or interact with the adrenergic system, enhancing the relaxation effect of isoprenaline. These findings collectively suggest that L. sativum exhibits antidiarrheal and antispasmodic effects through diverse mechanisms that vary by species. The extract appears to act via activation of potassium channels, inhibition of muscarinic and calcium channels, and potential phosphodiesterase inhibition. The highest potency was observed in rat tissues, which underscores the importance of using multiple species to fully understand the pharmacological profile and therapeutic potential of L. sativum.

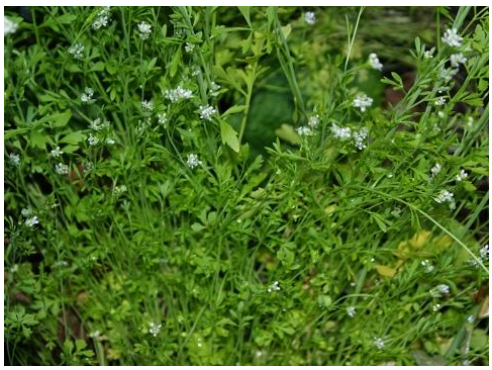

Figure 1- Lepidium sativum

Allium cepa

Allium cepa, commonly known as onion, belongs to the Liliaceae family and is widely used not only as a culinary staple but also for its medicinal properties. Onion is known for its antioxidant, spasmolytic, and antihypertensive activities, largely attributed to bioactive compounds present in its bulb and peel. One particular area of study is the antispasmodic effect of onion peel, which may offer therapeutic potential in managing smooth muscle spasms, particularly in the gastrointestinal tract. To examine the antispasmodic effects, onion peel powder was subjected to maceration in 70% ethanol for 72 hours to obtain an alcoholic extract. Researchers isolated a section of the terminal ileum from male Wistar rats and used it in an organ bath containing Tyrode solution at 37°C with 1 g of tension to measure contractions isotonically. The cumulative concentrations of the onion peel extract (0.1, 0.2, and 0.4 mg/ml) were tested for their effects on ileum contractions induced by high-potassium (60 mM KCl) and carbachol (10 µM), a muscarinic receptor agonist. The results demonstrated that the onion peel extract significantly reduced these induced contractions in a dose-dependent manner, with statistical significance ($P<0.0001$), indicating a strong antispasmodic effect. Notably, this effect remained consistent even after pre-incubating the ileum tissues with several inhibitors: propranolol (a β-adrenoceptor blocker), naloxone (an opioid receptor antagonist), L-NAME (a nitric oxide

synthase inhibitor), glibenclamide (a potassium channel opener blocker), and tetraethylammonium (a non-selective potassium channel blocker). These findings suggest that the extract's spasmolytic activity does not depend on pathways involving β-adrenoceptors, opioid receptors, nitric oxide production, or potassium channel activation, indicating a different mechanism of action. In a subsequent experiment conducted in a Ca2+-free Tyrode solution with high potassium (60 mM K+), the onion peel extract also significantly decreased contractions induced by the addition of CaCl2, again in a dose-dependent manner ($P<0.05$, $P<0.01$). This outcome indicates that the extract likely acts on calcium channels to inhibit calcium influx, which is essential for smooth muscle contraction. The bioflavonoid quercetin, known to be present in onion peel, is suggested as a key contributor to the observed spasmolytic effects. Quercetin has been shown in other studies to modulate calcium channels, potentially blocking calcium entry into smooth muscle cells and thereby reducing contraction. This mechanism may underlie the antispasmodic effects of onion peel extract and position it as a candidate for developing natural remedies for smooth muscle spasms. Overall, these findings highlight Allium cepa peel extract as a promising natural antispasmodic agent, acting independently of conventional receptor-mediated pathways and targeting calcium channel modulation for its therapeutic effects.

Figure 2 – Allium cepa

Zingiber officinale

Zingiber officinale, commonly known as ginger, belongs to the Zingiberaceae family and is well-known for its medicinal properties, including anti-inflammatory, digestive, and spasmolytic effects. To investigate its spasmolytic properties, an extract was prepared from dried ginger using methanol as the solvent. Dried ginger pieces were immersed in 70% methanol for 72 hours, allowing the active compounds to dissolve into the solvent. This process was repeated with fresh ginger rhizome in a new batch of methanol to ensure a comprehensive extraction of bioactive constituents. The combined solvent extracts were then filtered through a porous cloth and further refined using Whatman grade-1 filter paper. After filtration, the solvent was evaporated using a rotary evaporator, yielding approximately 126 grams of concentrated ginger extract (designated as Gd.Ex), which represents a 12.6% yield by weight. For experimental testing, Gd.Ex was dissolved in saline solution, which acted as a negative control with no effect on tissue contractility. The diluted extract solutions were then tested on isolated guinea pig ileum tissue, a commonly used smooth muscle model for evaluating spasmolytic activity. Small tissue sections (1-2 cm) were prepared and placed in organ baths containing a saline-based salt solution aerated with a gas mixture. A preload of one gram was applied to the tissues to mimic natural tension, and isotonic contractions were measured using the Harvard apparatus, which recorded changes in the tissues' length and contraction force. Prior to administering Gd.Ex or other test compounds, the tissues were allowed a 30-minute equilibration period. Stabilization was achieved using acetylcholine (ACh) at a standard concentration of 0.3 μM, a common agonist that induces contractions in smooth muscle tissue. A three-minute interval was maintained between the

applications of different test substances, allowing the tissue to return to baseline activity.

In contrast to the rabbit jejunum, which exhibits spontaneous rhythmic contractions, the guinea pig ileum maintains a quiescent, stable baseline without spontaneous contractions. This makes it particularly suitable for testing the effect of spasmolytic agents, as the absence of spontaneous contractions reduces background noise, providing a clear response to stimulant drugs and agonists.

To evaluate the spasmolytic effects of ginger extract, standard agonists like ACh, histamine, and potassium chloride (K+) were administered to the guinea pig ileum to induce contractions. ACh and histamine act on muscarinic and histamine receptors, respectively, to produce smooth muscle contractions, while K+ increases intracellular calcium levels, causing contraction through calcium-dependent mechanisms. The ability of Gd.Ex to inhibit these induced contractions would indicate its effectiveness as a spasmolytic agent, suggesting potential mechanisms involving the modulation of calcium channels, receptor blockade, or interference with smooth muscle contractile pathways. This setup provides a detailed and controlled environment for assessing the pharmacological effects of Zingiber officinale on smooth muscle relaxation.

Figure 3 – Zingiber offinale

Foeniculum vulgare mill

Foeniculum vulgare Mill., commonly known as fennel, is a medicinal plant from the Apiaceae family, widely recognized for its extensive pharmacological benefits. Known for its culinary and therapeutic uses, fennel exhibits a range of biological activities, including antispasmodic, antioxidant, anti-inflammatory, and antibacterial effects. These properties contribute to its use in traditional and modern medicine for treating various ailments, especially those related to the gastrointestinal and respiratory systems.

Studies on the antispasmodic effects of fennel have shown that its alcoholic extracts, particularly at concentrations of 2.5 and 10.0 mL/L, significantly relax smooth muscle tissues. Research has evaluated these effects in combination with other medicinal plants such as Melissa officinalis (lemon balm), Rosmarinus officinalis (rosemary), Mentha piperita (peppermint), Matricaria chamomilla (chamomile), Carum carvi (caraway), and Citrus aurantium (bitter orange). Using an isolated guinea pig ileum model, researchers found that fennel extract could inhibit smooth muscle contractions induced by spasmogens such as acetylcholine and histamine, both of which are compounds that naturally stimulate muscle contractions. Furthermore, the essential oils from fennel fruits, at concentrations of 25 µg/mL and 10 µg/mL, were tested for their effects on contractions induced by oxytocin and prostaglandins. The results revealed that these essential oils effectively reduced these contractions, indicating a strong antispasmodic effect. This activity suggests potential therapeutic applications for fennel in treating spasmodic conditions, including those associated with the gastrointestinal tract, such as irritable bowel syndrome and colic. These findings reinforce the traditional use of fennel in herbal medicine and support its potential as a natural remedy for managing muscle spasms and inflammation.

Figure 4 – Foeniculum vulgare

Lavandula angustifolia mill

Lavender (Lavandula angustifolia Process) could be a homegrown cure commonly utilized for gastrointestinal (GI) clutters; in any case, its pharmacological impacts on disconnected ileum compressions have however to be investigated. This consider examines the effect of hydroalcoholic extricate of L. angustifolia on confined ileum compressions and compares its impacts to those of loperamide. The hydroalcoholic extricate of the plant was prepared utilizing the permeation strategy, and the whole flavonoid substance was assessed through a colorimetric method. A fragment of rodent ileum was suspended in an organ shower filled with Tyrode's arrangement, kept up at 37°C beneath 1 g pressure and ceaselessly circulated air through with oxygen. The tissue was invigorated with KCl (80 mM), acetylcholine (ACh, 2 µM), and electrical field incitement (EFS). The impacts of the L. angustifolia extricate on ileum withdrawals were compared to those of loperamide. The hydroalcoholic extricate yielded 17% and contained a add up to flavonoid concentration of 185 µg/mL within the stock arrangement. Loperamide illustrated a concentration-dependent restraint of the ileum's contractile reaction to KCl, acetylcholine (ACh), and electrical field incitement (EFS). Additionally, the hydroalcoholic extricate of L. angustifolia (extending from 8 to 512 µg/mL) restrained ileum compressions actuated by KCl (IC50 = 88±21 µg/mL), ACh (IC50 = 119±251 µg/mL), and EFS (IC50 = 87±33 µg/mL) in a concentration-dependent way. The vehicle utilized within the tests did not altogether influence the withdrawals of the ileum. The discoveries of this consider recommend that the extrication of L. angustifolia shows an inhibitory impact on the smooth muscle of the rodent ileum at microgram concentrations. Subsequently, it is suggested that advanced investigation center on the isolation and recognizable proof of the dynamic components mindful of this movement.

Figure 5 – Lavandula angustifolia

RESULT AND DISCUSSION

Plants are key sources of bioactive compounds, historically used in medicine and now prominent in cosmetics, pharmaceuticals, and nutraceuticals, with a market predicted to reach USD 86.74 billion by 2022. GI disorders, prevalent in children, impact their physical and emotional well-being, with symptoms like chronic abdominal pain affecting daily life. Common synthetic antispasmodics, while effective, pose side effects, particularly concerning for children. Ayurveda provides safer, plant-based alternatives, including garden cress, onion, ginger, fennel, and lavender, which relieve GI issues without adverse effects. This highlights the need for further research into natural treatments. Antispasmodic herbal plants offer natural GI relief through diverse mechanisms. Lepidium sativum activates potassium channels and inhibits muscarinic and calcium channels, Allium cepa modulates calcium channels to reduce contractions, Zingiber

officinale acts as a natural spasmolytic, Foeniculum vulgare mitigates spasms induced by acetylcholine and histamine, and Lavandula angustifolia inhibits contractions similar to loperamide. These plants hold promise for GI disorder treatment, though further species-specific studies are needed.

CONCLUSION

In conclusion, plants are a vital natural source of bioactive compounds that hold immense potential in medicine, nutraceuticals, and cosmetics. Traditional plant-based remedies have long been used in folk medicine for treating various ailments, and the demand for plant preparations is expected to increase, with the market value predicted to reach USD 86.74 billion by 2022. This growth reflects the interest in phytochemicals across industries. Leaves, often considered agricultural waste, are particularly rich in bioactive compounds, offering a valuable resource for Nutra-pharmaceutical applications. Furthermore, gastrointestinal disorders, especially in children, underscore the need for safe, effective treatments. Synthetic antispasmodics often have side effects, which emphasizes the value of natural alternatives used in Ayurveda, such as ginger and fennel, for managing digestive issues. Overall, as scientific evidence grows, the use of plant-based remedies will likely expand, offering holistic and accessible options for health and well-being. They identify numerous plants that effectively address various gastrointestinal issues without causing side effects such as *Lepidium sativum* (garden cress), *Allium cepa* (onion), *Zingiber officinale* (Ginger), *Foeniculum vulgare* (Fennel), *Lavandula angustifolia mill* (lavender).

Future scope:

The prospects for the antispasmodic activity of herbal plants are highly promising, driven by an increasing demand for natural therapies in managing gastrointestinal (GI) disorders, muscle spasms, and related ailments. Numerous plants, such as *Lepidium sativum* (garden cress), *Allium cepa* (onion), *Zingiber officinale* (ginger), *Foeniculum vulgare* (fennel), and *Lavandula angustifolia* (lavender), exhibit antispasmodic effects through mechanisms like calcium channel blocking, potassium channel modulation, and muscarinic receptor inhibition. These mechanisms offer therapeutic benefits, including reduced GI cramping, smoother digestion, and relief from colic and muscle spasms, often with fewer side effects than synthetic drugs. Prospects depend on clinical trials to establish efficacy, safety, and optimal dosing, aiming to provide standardized, effective, and safe herbal options for patients seeking alternatives to synthetic drugs

Benefits: These plants' natural composition often leads to better tolerability, fewer side effects, and holistic benefits, as many also exhibit anti-inflammatory and antioxidant properties. Their multifunctional nature makes them attractive in complementary and alternative medicine, especially for patients seeking plant-based treatments for mild to moderate GI discomfort.

Limitations: Despite their potential, herbal antispasmodics face limitations such as variability in active compound concentration, potential interactions with other medications, and a lack of standardized dosages. Furthermore, more clinical research is needed to confirm efficacy and safety in humans, as most studies are preclinical or animal-based. Addressing these challenges through standardized extracts, well-designed human trials, and clear dosing guidelines will be crucial for successfully integrating herbal antispasmodics into mainstream therapeutics

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