INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES
[ISSN: 0975-4725; CODEN(USA): IJPS00]
Journal Homepage: https://www.ijpsjournal.com

OPEN ACCESS

Review Paper

Phyto-Therapeutic Strategies in The Management of Anorexia: An Evidence-Based Review

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ARTICLE INFO

Published: 29 May 2026
Keywords:
Anorexia, Appetite stimulants, Herbal medicine, Nutritional supplementation, Micronutrient replacement, Functional foods – Nutraceuticals, Malnutrition, Nutritional rehabilitation , Patient compliance
DOI:
10.5281/zenodo.20443454

ABSTRACT

Anorexia, the loss of appetite and the decrease in food intake, is a major clinical issue, which results in malnutrition, immunity impairment, and poor quality of life. Modern drug therapy is not always effective and is also associated with side effects, which poses a need to seek safer alternatives that are of plant origin. This review examines the therapeutic potential of medicinal plants and their bioactive components in stimulating appetite with special attention to traditional use, mechanistic understanding and recent experimental results presented in modern research. The scientific databases such as PubMed, Google Scholar, and ScienceDirect were searched to collect the relevant literature. Ethnopharmacological information, experimental and clinical reports regarding the use of herbs in the treatment of anorexia and appetite regulation were evaluated. There are a number of aromatic and bitter herbs that have been shown to stimulate appetite in a variety of ways. Plants that contain volatile oils, like Zingiber officinale (ginger), Mentha piperita (peppermint), Cinnamomum zeylanicum (cinnamon), Elettaria cardamomum (cardamom), Foeniculum vulgare (fennel), and Cuminum cyminum (cumin), are principally active by their olfactory and gustatory stimulation, which increases salivation, gastric secretions and hunger signals. Bitter principles of gentiana lutea (gentian) and similar herbs stimulate digestive reflexes by stimulating the taste receptors. Moreover, long-term appetite and nutrition balance is promoted by adaptogenic plants (i.e., Withania somnifera, ashwagandha) and nutrient-dense seeds (i.e., Cucurbita pepo, pumpkin) taken orally.The use of herbal interventions is a promising and multifaceted perspective of the treatment of anorexia, which can stimulate appetite in the short term and effectively provide nutrition support in the long term. Although preliminary results are promising, clinical trials should be conducted on a well-designed basis in order to confirm the efficacy, the optimal dosage forms, and the safety profiles.

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Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

INTRODUCTION

Anorexia which can in general sense be described as the loss or loss of appetite is a very critical clinical symptom with significant physiological and health consequences. It is the opposite of anorexia nervosa, a particular psychiatric condition that is marked by a strong fear of gaining weight, distorted body image, and self-induced starvation. Although anorexia nervosa is a complicated eating disorder that must be managed by specialists, using a combination of psychology and medicine, anorexia as a symptom appears in various situations, including infections, chronic illness, medications, and nutritional deficiencies, which are manifestations of impairments in the normal appetite regulation processes [1][2]. This is the most important distinction that can be understood to diagnose and stratify treatment.

Anorexia has a physiological effect on some of the important body functions. The appetite is a prominent controller of the food intake, which subsequently influences the digestion, absorption of nutrients, metabolic homeostasis, and energy balance. Malnutrition, muscle wasting, immunosuppression and delaying of illnesses are caused by insufficient consumption of nutrients due to loss of appetite [3][4]. Clinically, anorexia can be linked to negative effects like slow growth, loss of cognitive abilities, susceptibility to infections, and high risk of mortality especially in vulnerable groups like children, the elderly and those with chronic diseases [5][6]. The symptom therefore, is a marker and mediator of ill health.

Anorexia is a serious health burden throughout the world. The World Health Organization (WHO) and UNICEF report that malnutrition as a result of poor dietary consumption is the most significant cause of morbidity and mortality on the planet, and that a significant number of children suffer stunting and wasting as a result of poor appetite and feeding problems [7][8]. A high incidence of anorexia-related disorders is found in low and middle-income nations but is also being noted in developed nations because of chronic illness and ageing populations [8][9]. This is a global burden, and therefore effective identification, prevention, and management strategies are required.

In terms of public health, the effect of anorexia on malnutrition plays a leading role in child growth failure, impaired cognitive development and non-optimal chronic disease outcomes including cancer, heart failure and chronic kidney disease [10][11]. Treatment of anorexia is therefore a key issue in enhancing health status and health care expenditure. The control of appetite is a complex, neurohormonal process incorporating signals of the gut-brain axis, hormonal action such as ghrelin and leptin, and central nervous system regulation [12]. The pathogenesis of anorexia is based on the disruption of such pathways, which is the object of the therapeutic effort.

The objective of this review is to explain the complicated processes of appetite regulation as they are observed in anorexia and to compare the existing pharmaceutical interventions with the new herbal and natural ones. The article attempts to create gaps in knowledge, dismantle current paradigms, and provide recommendations regarding future research that can maximize clinical management and population health interventions by synthesizing new evidence. This multifactorial etiology and wide-ranging implications of anorexia necessitate such all-inclusiveness in the understanding of the disorder to come up with effective, accessible, and safe treatment modalities to reduce its global health effects.

Physiology of the appetite regulation.

The regulation of appetite is a complicated physiological entity that is controlled by both central and peripheral mechanisms, comprising metabolic, hormonal, neural and environmental

cues to achieve energy homeostasis. The main center of appetite is located in the hypothalamus which is an important part of the brain that houses interconnected groups of nuclei like the arcuate nucleus (ARC), ventromedial hypothalamus (VMH), and lateral hypothalamus (LH). Hunger and satiety are controlled by hypothalamic centers that have complex neuronal circuits to sensor various metabolic cues [13][14][15].

Central Mechanisms

Arcuate nucleus plays a very crucial role in controlling appetite. It contains two kinds of neurons, one of them makes you feel hungry and the other one makes you feel full. With these neurons other parts of the brain are signaled by the neurons and they assist in controlling hunger and fullness depending on the amount of energy your body holds. The VMH is called the satiety center and when damaged, individuals overconsume food. The LH is referred to as the hunger center and it assists in initiating eating. The combination of these parts of the brain dictates the amount that we should eat depending on our energy requirements.[14][15][16][17]

Peripheral Mechanisms and Gut-Brain Axis.

Digestive tract signals play a significant role in informing the brain of whether we are full or hungry. Leptin, ghrelin, CCK, PYY and GLP-1 are hormones that regulate our appetite by acting on areas of the brain. Ghrelin is what the stomach produces predominantly and makes us feel hungry. Leptin, which is produced by the fat tissue, demonstrates that we possess sufficient energy and it suppresses our appetite. Following food intake, the hormones such as CCK, PYY, and GLP-1 are secreted in the small intestine and colon. They reduce the rate at which fast food moves out of the stomach, make us feel full, and assist in reducing the amount we consume.[13][14][15][18][19]

Neurotransmitters and Metabolic Signals

Circuit neurotransmitters play a role in hypothalamic appetite. When stimulated by serotonin (5-HT), the receptors located on POMC neurons and other related limbic areas usually decrease appetite, which controls mood and feeding response [20][21]. The dopamine controls the motivation to eat and to be rewarded with the dopaminergic cells of the ARC and LH being involved in the regulation of the feeding drive by using receptor subtypes-specific actions [22]. Neuropeptide Y is a powerful orexigenic neuropeptide that gets released as negative energy balance that sparks eating and decreasing energy expenditure [14][15]. Hypothalamic neurons are also influenced by metabolic signals like insulin and glucose and these signals regulate the appetite based on the nutrient availability [14][21].

Exposure to Psychological, Nutritional, and Environmental Factors.

Psychological disorders such as stress, depression, and anxiety affect the appetite through a change in central neurotransmission and changes in hormones, which tend to suppress appetite or to eat emotionally [23][24]. Nutritional status and macronutrient intake drives the release of gut hormones and hypothalamic sensitivity thereby influencing hunger and satiety signals. The interaction between environmental factors, including food availability, social environment, and behavioral learning, and physiological processes which influence feeding behavior is dynamic [14][23][24].

Disruption in Anorexia

In anorexia these pathways that are carefully controlled are dysregulated. It has been demonstrated to be associated with altered ghrelin signaling with high levels of plasma ghrelin, indicating the presence of central insensitivity involved in persistent anorexia [25][26]. The structural and functional alterations in the

populations of hypothalamic neurons that control appetite in anorexic patients are observable [25]. A further consequence of disregulation of neurotransmitters such as serotonin and dopamine is negative effect on appetite loss by disrupting reward and motivational pathways [22][20]. This disruption leads to the clinical manifestation of poor food consumption, malnutrition, hormonal disbalance, and aggravation of the prognosis of diseases.

Causes of Anorexia

Anorexia, which refers to loss or serious lack of appetite, is a complex situation unlike anorexia nervosa, the latter being a patient-specific mental disorder of self-induced starvation due to a distorted body image and a strong fear of gaining weight. Although anorexia nervosa is a psychiatric diagnosis, anorexia as a symptom exists in a wide variety of clinical and environmental situations, indicating the presence of physiological or psychosocial disorders [34][35]. It is important to know the wide range of the causes of anorexia as a basis of proper diagnosis, management and community health

Psychological Causes

Appetite is greatly influenced by psychological factors. Clinically, neurochemical and neuroendocrine disorders (e.g., dys-regulation of serotonin and dopamine mechanisms) which inhibit appetite and change feeding behave are linked to depression, anxiety, and chronic stress [44][45]. Food related disorders such as anorexia nervosa and bulimia nervosa are leading psychiatric etiologies with complicated underlying psychopathology that results in disastrous eating behaviors [34][35]. Moreover, the bidirectionality between the mental state and the appetite can be taken into consideration via the fact that the psychological distress due to severe illness may intensify the anorexia [46].

Nutritional Causes

Another cause of anorexia that is under-appreciated is micronutrient deficiencies. Lack of zinc, vitamin A, vitamin B complex, and iron may harm the sense of taste, lower secretions in the mouth, and interfere with the production of neurotransmitters involved in appetite control [47][48]. Malnutrition itself forms its own vicious cycle in that insufficient nutrient consumption further reduces the hunger signal, further fueling anorexia specifically in resources restricted environments and in at risk population groups [49].

Ages and Populations at risk.

The interaction of these causes takes different forms with different age groups. Anorexia as a result of infection, malnutrition, and micronutrient deficiencies is especially dangerous to children and their development, making them particularly vulnerable to it [49][52]. Older groups tend to experience multifactorial anorexia as a result of chronic illnesses, polypharmacy, sensory issues and psychosocial elements [54][55]. Compounded anorexia is common in patients with chronic conditions because of the interactions between medical, psychological and treatment factors and they need multidisciplinary strategies [37][40].

Global Burden

The anorexia-induced malnutrition is a huge problem worldwide. In line with the WHO and UNICEF reports, undernutrition is a major cause of morbidity and mortality among children under the age of five with anorexia being a component factor [52][56]. Anorexia leads to malnutrition, which predisposes people to infections, slows down recovery and exacerbates chronic disease outcomes on a global level [39][40]. To tackle anorexia in the context, it is critical to enhancing health equity and fulfilling the global nutrition goals.

Current methods of treatment and limitation

The existing treatment options in the management of anorexia have included multidisciplinary management, which is dependent on the cause of anorexia which is a symptom of anorexia nervosa brought about by a loss of appetite and not a complex psychiatric eating disorder, which is anorexia nervosa.

Pharmaceutical Interventions.

Synthetic progestogen Megestrol Acetate possibly has an effect on the stimulation of appetite due to hypothalamic modulation and inhibition of cytokines. It has clinical efficacy in weight gain in cachexia in cancer, HIV and chronic diseases. But long-term use is because of adverse effects like edema, hypertension, and thromboembolism [57][58].

The Cyproheptadine is a serotonin and histamine antagonist which suppresses the satiety cues increasing the appetite. It has modest effects, and has side effects such as sedation, anticholinergic symptoms, which can negatively affect tolerability [57][58].

Corticosteroids also enhance appetite through anti-inflammatory and neuroendocrine mechanisms but have limitations such as immunosuppression, glucose intolerance, osteoporosis and mood changes hence should be used in the short term [57][58].

Dronabinol in cannabinoids, like cannabinoid receptors, stimulates appetite and decreases nausea but due to psychoactive side effects and regulatory issues, it has not been widely adopted [57][58].

These agents have short term effects with little long term effectiveness and safety profiles. Adverse reactions and patient compliance are still both important impediments [57].

Nutritional Management

The use of dietary supplementation, micronutrient replacement, and assisted feeding methods are core components of the treatment of anorexia through nutritional rehabilitation:

Dietary Supplementation is concerned with replacement of deficits with high-energy protein consumption.

Micronutrient Replacement especially the zinc and vitamins, reduce typical deficiencies that aggravate the loss of appetite and metabolic malfunction [60].

Complementary and Herbal Therapies.

Traditionally herbal medicines are used to stimulate appetite, and their composition and dose are vastly heterogeneous, and clinical trials are restricted by the heterogeneity of methodology [62].

Bioactive-enriched functional foods are under investigation, although no strong evidence has as yet emerged [63].

Herbal and nutritional intervention

Herb / Extract	Biological Name	Uses / Clinical Indications	Safety & Tolerability
Gentian root	Gentiana lutea, G. acaulis	Stimulates appetite, aids digestion, treats indigestion, flatulence, appetite loss	Generally well tolerated in moderate doses; avoid in peptic ulcers, pregnancy; may cause mild GI upset, headache
Wormwood	Artemisia absinthium	Appetite stimulant, digestive aid, anthelmintic, antimicrobial	Contains thujone, neurotoxic at high doses; avoid prolonged/high dose; can cause seizures and allergic reactions

Herb / Extract	Biological Name	Uses / Clinical Indications	Safety & Tolerability
Ashwagandha	Withania somnifera	Adaptogen, stress relief, immunomodulator, energy, possible appetite stimulant	Generally safe at recommended doses; possible GI upset, drowsiness; avoid pregnancy; rare liver injury reports
Trikatu (mixture)	Piper nigrum, P. longum, Zingiber officinale	Digestive enhancer, bioavailability enhancer, appetite stimulant	Well tolerated with food; excessive use may cause mucosal irritation, burning sensation; avoid in gastritis
Dandelion	Taraxacum officinale	Mild appetite stimulant, diuretic, liver tonic	Safe as food/dietary supplement; allergy risk in Asteraceae sensitive; caution in gallbladder disease
Vidanga	Embelia ribes	Anti-parasitic, digestive stimulant	Safe in traditional doses; avoid in pregnancy; mild GI upset or allergy possible
Cinnamon	Cinnamomum verum, C. cassia	Antimicrobial, antioxidant, digestion aid, mild appetite stimulant	Safe as spice; high doses may cause allergic dermatitis or liver toxicity (cassia cinnamon coumarin content)
Clove	Syzygium aromaticum	Antimicrobial, analgesic, antioxidant, appetite stimulant	Safe as spice; avoid large doses of clove oil internally; may cause mucosal irritation
Pumpkin seed extract	Cucurbita pepo	Anti-parasitic, GI support, mild appetite stimulant	Generally safe; rare allergy; safe in dietary doses
Ginger	Zingiber officinale	Carminative, antiemetic, appetite stimulant, anti-inflammatory	Safe in culinary doses; high doses linked to heartburn, GI irritation, bleeding risk

- **Nutritional support** (zinc, proteins, tryptophan from pumpkin seeds) corrects deficiencies linked to anorexia.
- **Adaptogenic effect** (Ashwagandha) reduces stress-induced appetite loss and supports digestion.
- **Digestive stimulation** (Trikatu) enhances bioavailability of nutrients and triggers hunger signals**.**

FUTURE PERSPECTIVES

According to recent studies, herbal interventions have a potential to treat anorexia via several pathways, i.e. appetite stimulation, digestive, and metabolic. On the basis of these findings, a new formulation plan can be developed which focuses on the combination of aromatic, bitter and nutritive herbs. Volatile oil-rich aromatic herbs can potentially stimulate appetite, and bitter herbs may act by stimulating digestive reflexes and increasing gastric secretions. The adaptogenic and

nutrient-rich herbs are long-term aids to energy balance and nutrition.. This framework provides a flexible and scientifically sound development of future herbal interventions with regards to anorexia by the concentration on the mechanistic complementarity, safety, and phytochemical rationale without revealing proprietary formulations.

CONCLUSION

Herbal treatments are a promising and versatile way of addressing appetite loss and anorexia. The use of aromatic, bitter and nutritive herbs, as evidenced by both traditional medicine and modern research, is effective in increasing appetite, improving digestive activity, and maintaining nutritional status. The effect of herbs may be through bitter compounds and nutrient-rich herbs may lead to long-term metabolic and digestive reflexes. Even though the initial results are promising, more comprehensive clinical trials need to be performed to confirm that it is effective, reduce dosage forms, and make sure it is not harmful. In sum, a multimechanistic, vegetarian approach would be a scientifically-based, safe, and flexible construct that can be used in future studies and therapy in the context of enhancing appetite.

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HOW TO CITE: Jyoti Tiwari, Khinayaram Choudhary, Dr. Pragnesh Patni Phyto-therapeutic Strategies in the Management of Anorexia: An Evidence-Based Review, Int. J. of Pharm. Sci., 2026, Vol 4, Issue 5, 7838-7847, https://doi.org/10.5281/zenodo.20443454