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Multidimensional Impacts on *Bryophyllum Pinnatum* for the Potential of Obesity: A Review

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Abstract

Global public health concerns related to obesity are growing. Several comorbid illnesses, including cardiovascular disease (CVC), gastrointestinal disorders, type 2 diabetes (T2d), joint and muscle disorders, respiratory difficulties, and psychological disorders, are significantly more common in obese patients. The widespread misconception that obesity stems solely from a lack of self-control is gradually losing its stigma as awareness about fat-related issues grows. Instead of synthetic drugs herbal or medicinal plants are much beneficial in the treatment of obesity. Bryophyllum pinnatum leaves have been employed as an antibiotic in traditional medicine. So, in this paper we reviewed that plant have various pharmacological effects on the body with very less side effects and their active phytoconstituents have an soothing effect to get rid of obesity.

Keywords: Obesity, synthetic drugs, medicinal plants, phytoconstituents, *Bryophyllum Pinnatum*

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INTRODUCTION

Obesity is a rising global public health concern, placing individuals at a heightened risk of developing various comorbid conditions, such as cardiovascular diseases, gastrointestinal disorders, type 2 diabetes, joint and muscular disorders, respiratory issues, and psychological disorders. These conditions can significantly impact daily life and increase mortality risk. Obesity is associated with numerous health conditions; however, even modest weight loss can help reduce the risk of cardiovascular disease, diabetes, obstructive sleep apnea, high blood pressure, and many other comorbidities. A proportionate little and straightforward reduction in weight, for example, of roughly 5%, can enhance patient outcomes & may act as a catalyst for more distant change, with lasting weight loss achieved through a chain of steps for weight loss stages. An important job that nurses perform is helping patients lose weight. By determining the patient's risk, setting realistic weight-loss goals, encouraging and supporting them, and giving them the knowledge and treatment resources they need to help them lose weight, we can help them maintain their new weight with tools for an organized lifestyle [1].

The prevalence of obesity has surged significantly over the past decade, driven by changes in dietary habits and physical activity patterns [2, 3]. It is currently predicted to be over 40% and with the corona virus disease 2019 (COVID-19) pandemic, this frequency is expected to rise even higher [4, 5]. Global recognition exists for obesity as a component of the global syndetic, a set of health problems that will impact people and the environment in the future. Obesity is classified under nutrition and climate change [6, 7] Environmental variables that are global acknowledged to be responsible for the sharp rise in obesity International include the use of antiepileptic and psychiatric medications, sedative, circadian desynchronization, chronic stress, and increasing access to energy-dense foods combined with loss physical activities [8–12].

The widely held assumption that obesity results from a lack of self-control is less stigmatized than an increase in body mass. It's becoming recognized that obesity is a chronic degenerative disease. Additionally, this promotes funding for basic and applied research, provides insurance companies and healthcare providers with the necessary resources to establish obesity control initiatives, and forces pharmaceutical companies to offer body weight management programs [13–16]. However, because obesity is influenced by a wide range of complex elements including genetic, physiological, behavioral, sociocultural, and environmental factors, therapeutic options for people with obesity are currently insufficient [17–20]. The widely spread misconception that obesity is the result of a lack of self-control is becoming less stigmatized as obesity is becoming admitted as a chronic degenerative illness. This also encourages funds for scientific clinical research, gives healthcare providers and insurance companies the pay for to create obesity control programs and pushes pharmaceutical companies to provide body weight management plans. However, because obesity is influenced by a wide range of complex elements including genetic, physiological, behavioral, sociocultural, and environmental factors, therapeutic options for people with obesity are currently insufficient [21–24].

Changing lifestyle is the first step in every obesity treatment program. Treatment for obesity must include both a reasonable exercise program and a better diet. Nevertheless, cumulative data indicates that over half of the weight lost throughout the 2-year period was gained again by most patients, who are unable to sustain this lifestyle [25–27], despite intermixed trials showing a >8% lose in weight in the first years. Pharmacological therapy needs to be taken into consideration to help people with fat to lose enough weight. A pharmacological strategy ought to be employed based on the kind of obesity and the safety and effectiveness of each medication. Food and Drug Administration, state that for a product to be considered an effective anti-obesity medication, it must cause at least 5% mean weight loss, it shows a statistically significant difference from the placebo group, and after a year of treatment, more than 35% of patients must explicitly lose weight of at least 5% [28–31].

Additionally, an anti-obesity drug must improve glycemic control, blood pressure, cholesterol, and other cardio metabolic markers, according to FDA regulations. When combined with lifestyle modifications, most anti-obesity medications cause an average 5–15% reduction in body weight [32].

The BMI group for defining obesity varies by age and different gender in infants, children and adolescents.

Adults

For adults, World health organization defines overweight, and obesity as follows:

- Obesity is a BOODY MASS INDEX greater than or equal to 25; and
- For children, age needs to be considered when defined as obese or obesity.

Children Under 5 Years of Age

For children under 5 years of age:

- The weight-for-height of obesity is more than two standard deviations over the median of the WHO Child Growth Standards.

- Weight-for-height, obesity is defined as being more than three standard deviations above the World Health Organization's Child Growth Standards median.

Children Aged Between 5 and 19 Years

- A BMI for age that is more than one standard deviation above the WHO Growth Reference median is considered obese.
- Overweight is greater than 2 standard deviations above the WHO Growth Reference median [33–36].

Types of Obesity

Depending on the Distribution of Fat in the Body, Obesity can be Categorized into Three Types:

- *Peripheral Obesity:* Excess fat accumulation primarily in the thighs, buttocks, and hips.
- *Central Obesity:* Excess fat accumulation concentrated in the abdominal region.
- *Combination Obesity:* A pattern of fat accumulation that includes both peripheral and central regions.

Depending on the Association with other Diseases, Obesity can be Classified into the Following Types:

- *Type 1 Obesity:* This type of obesity is primarily caused by excessive calorie intake and insufficient physical activity, without being linked to any underlying disease.
- *Type 2 Obesity:* This type of obesity is linked to various diseases, including hypothyroidism, polycystic ovarian syndrome, insulinoma, certain internal secretion disorders, and Cushing's syndrome. It is characterized by abnormal weight gain, even with minimal food intake.

Depending on the Size and Number of Fat Cells, Obesity can be Classified into the Following Types:

- *Adult-Type Obesity:* In this type of obesity, the increase in fat is primarily due to the enlargement of fat cells, typically occurring in middle adulthood.
- *Child-Type Obesity:* In this type of obesity, the number of fat cells increases and it is difficult to reduce their number, often starting during childhood.

Role of Adipose Tissue

The primary source of free fatty acids (FFA) for energy consumption and heat production during the postprandial fasting state is adipose tissue, which is essential to animal survival [37]. Mammals have two forms of adipose tissue: Brown adipose tissue (BAT) and white adipose tissue (WAT) are the main sources of FFA and most of the body's total fat, which are used as energy substrates by oxidative phosphorylation of adenosine triphosphate (ATP). High-voltage connections. On the other hand, heat is produced by non-oxidative phosphorylation and supplied by BAT. Presently held beliefs suggest that resident tissue macrophages release anti-inflammatory cytokines and adipocytes store fats and control metabolic balance under normal WAT circumstances. According to research, metabolic excess primarily causes increased stress to the intracellular organelles and cells of obese WAT [38, 39]. A chemotactic stimulus for macrophage entry and accumulation is also provided by the rise in local extracellular FFA concentrations brought on by the increase in basal lipolysis that obesity induced Inflammation of the adipose depot caused by obesity begins with the recruitment of macrophages into adipose tissue [40–47]. Chemokines, such as monocyte chemo attractant protein-I (MCP-I), are released by adipocytes in response to overnutrition, creating a chemotactic gradient that draws monocytes into adipose tissue. A body of research has revealed that an inflammatory mediator produced from adipose tissue TNF-α (tumor necrosis factor) plays a role in insulin resistance linked to obesity [40–42]. Additional research revealed that TNF-α expression is elevated in the fat tissue of obese people, and that there is a correlation between its level and adiposity. Additionally, fat tissue can secrete angiotensin II, which increases the activity of NADPH oxidase. In adipocytes, the primary pathway for the formation of ROS is NADPH oxidase [43–45].

Biology of Obesity

Endocrine and neurological factors that ultimately affect energy intake and expenditure are thought to play a major role in controlling body weight, according to a wealth of research. Numerous factors are blamed in the pathogenesis of obesity, such as leptin, ghrelin adipokinin, and rennin angiotensinogen. A review of the literature indicates that being overweight is one of the primary risk factors for cardiovascular diseases (CVD). Higher risk of hypertension, hyperglycemia, and dyslipidemia, declare it to be the metabolic syndrome (Redinger, 2007). Further, it has been discovered that obesity is linked to a chronic inflammatory response, which is characterized by aberrant adipokine synthesis and the activation of pro-inflammatory signaling pathways that induce several molecular indicators of inflammation [46].

Obesity is measured by the BMI, despite the urgent of safe therapeutics the synthetic drugs are consumed which are available in the market, the current efforts for the advance of these drugs are still unsatisfactory and synthetic drugs have low cost and high side effects. This is due to adverse effects related to a drug which leads to major problems like organ damage. So, the current approach has focused on natural sources that have been beneficial and effective to manage obesity and other related problems as well as reduce weight gain with less side effects [47, 48].

It is a serious, chronic, prevalent, relapsing disorder of 21st century and is one of the leading causes of preventable deaths

REVIEW OF LITERATURE

Obesity is a multifaceted condition resulting from excess fat accumulation in adipose tissue, the liver, skeletal muscle, and other areas, affecting lipid and carbohydrate metabolism (WHO, 2011). Obesity is considered one of the most serious global health concerns due to its potential role as a risk factor for hypertension, CVD, type 2 diabetes, nonalcoholic fatty liver disease, metabolic syndrome, stroke, and cancer [25, 26] Obesity is a serious, chronic, prevalent, relapsing disorder of 21st century and is one of the leading causes of preventable deaths Prevention and treatment of this problem is an important deal for health systems, whose aim is to reduce the obesity and related issue. Almost all age groups and socioeconomic classes are affected by obesity, which is a complex disorder with significant social and psychological aspects. At least 300 million adults worldwide are clinically obese, and over one billion adults are overweight worldwide (WHO, 2009). At the individual level, most of the causes of obesity are assumed to be explained by the combination of high food energy consumption and inactivity [49].

Plant Profile

Bryophyllum pinnatum (B. pinnatum)

The term *B. pinnatum* comes from the Latin for "feathered, winged," and is derived from the Greek word bryo, which means to sprout, and phyllon, which is a leaf that can be propagated by leaf cutting. The environmental plant *B. pinnatum* belongs to the family of pine plants. It is commonly used as a medicine, primarily for urinary stones, in several parts of India and other countries. It tastes bitter, is astringent, has a sweet after-digestive effect, and is highly potent. Its ability to heal wounds and promote hemostasis is well established. Plants are used worldwide to treat a variety of ailments, including abscesses, skin conditions, asthma, colds, and hypertension. It is widely grown and used in tropical America, Madagascar, Asia, Hawaii, and tropical Africa as well as in India, China, and Australia as traditional medicine. The bark and leaves have carminative, analgesic, astringent, bitter tonic, and diarrheic properties. The leaves of this plant have been employed as an antibiotic in traditional medicine. Powerful antihistamine and anti-allergic activity, antifungal, antiulcer, anti-inflammatory, analgesic, antihypertensive, and anti-inflammatory [50–52].

Morphology

Grows to a height of 1–1.5 meters, *B. pinnatum* is a perpetual extensively herb. The stem is often branching, hollow, and four-angled. The opposing, succulent, decussate leaves are 10–20 centimeters

long. The long-petioled, 3–7 foliate upper leaves are more complex than the simpler lower ones. They are meaty, dark green in color with a recognizable scalloped, and red-trimmed edge. Leaf blade compound, pinnately arranged, 3–5 leaflets, and 10–30 cm. There are vegetative buds on the leaves that can take root. Numerous pendulous flowers resemble bells. It possesses hot strength and tastes sour, astringent, and sweet after digestion [53].

A ridge encircling the stem connects the petioles. The petals have a reddish-purple color, with inflated, octagonal bases, and triangular lobes. Green at base of filaments, pinkish beneath anthers. Anthers are black and hastate, styles green (Figure 1a-b). The persistent papery calyx and corolla enclose the fruit. The smooth, tiny seeds (Table 1).

Figure 1. (a) Whole plant, (b) Leaves.

Trivial Names

- *Hindi:* Zakhmhaiyat, Patharchatt
- *English:* Air plant
- *Sanskrit:* Parnabeeja, Asthibhaksha
- *Telugu:* Ranapala
- *Kannada:* Gandukalinga, Kadu basale
- *Malayalam:* Elamarunga
- *Tamil:* Rana Kalli

Preliminary Phytochemical Analysis of *B. pinnatum*

Phytochemical screening of the methanolic extract revealed the presence of alkaloids, flavonoids, tannins, saponins, phenols, terpenoids, steroids, fats, and other compounds. The results were shown in Table 2.

Sample Preparation

The samples were dried at room temperature for 3 weeks, after which they were ground into a fine powder using a grinding machine.

Extraction

To perform the aqueous extraction, the weighing scale was reset to zero, filter papers were placed on the balance, and 0.5 g of the sample was carefully weighed and transferred into a reagent bottle. To facilitate the extraction, 10 milliliters of distilled water were added to the sample. Following a few minutes, appropriate filtration was performed using filter paper, and the filtrate's contents, including tannins, alkaloids, saponins, glycosides, terpenoids, flavonoids, steroids, and phenols, were measured [54].

Test for Tannins

- Extract (0.1 g).
- Stir with 10 ml of distilled water and then filter.
- Add Few drops of 1 % ferric chloride solution added to 2 ml of each filtrate presence of a blue-black or blue-green precipitate indicated presence of tannins.

Table 1. Herbal plants in the management of obesity.

S.N.	*Plant Name*	Family	Parts of Plant Used
1	*Achyranthus aspera*	Amaranthaceae	Root, seed, leaf, whole plant
2	*Berberis aristate*	Berberidaceae	Root, stem, fruit
3	*Cedrus deodara*	Pinaceae	Heartwood oil
4	*Coriandum Sativum*	Umbelliferae	Seed
5	*Camellia thea*	Leaves	Seed
6	*Camellia thea*	Leaves	Seed
7	*Emblica officinalis*	Phyllanthaceae	Fruit
8	*Moringa oleifera*	Moringaceae	Leaves
9	*Piper nigrum*	Fruits	Fruit
10	*Hibiscus sabdariffa*	Malvaceae	Calyces
11	*Cuscuta reflexa*	Convolvulaceae	Whole plant
12	*Emblica officinalis*	Phyllanthaceae	Fruit

Table 2. Results of phytochemical screening.

S.N.	Phytoconstituents	Present (+) / Absent (-)
1	Alkaloids	+
2	Flavonoids	+
3	Tannins	+
4	Saponins	+

Test for the Alkaloids

- A quantity of the extract (0.1 g).
- Dissolved individually in diluted Hydrochloric acid and filtered.
- Presence of alkaloids and give yellow colored precipitate.

Test for Saponins

- A quantity of each extract (0.1 g) was boiled with 5 ml of distilled water and filtered.
- Shaken vigorously for about 5 minutes.
- Persisted warming was taken as evidence for the presence of saponins.

Lead Ethanoate Test for Flavonoids

- A quantity (0.1 g) of each extract was dissolved in water and filtered.
- A solution for about 3 ml lead ethanoate solution was added.
- Precipitate indicated the presence of flavonoids.

Test for Terpenoids

Each extract (0.1 g) was dissolved in ethanol, and 1 ml of acetic anhydride was added, followed by the addition of concentrated H_2SO_4. A color change from pink to violet indicated the presence of terpenoids [55, 56].

Result

Antimicrobial Activity

Different leaf extracts of *B. pinnatum* (aqueous, methanol, etc.) exhibited varying antibacterial activities against the tested gram-positive and gram-negative bacteria. Among the extracts, the

methanol extract demonstrated significant antibacterial activity against the control strains of *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and *Enterococcus faecalis*, comparable to the control antibiotic, ciprofloxacin. The extract from the squeezed leaves of *B. pinnatum* exhibited significant effects on several gram-positive and gram-negative organisms. In contrast, other extracts showed moderate to weak activity against the tested bacteria.

Wound Healing Property

The study reports on the effects of *B. pinnatum* leaf extracts petroleum at a dose of 400 mg/kg orally on the healing of excision wounds. The extract was applied topically to the excision wound model for 21 days until the eschar formed. The breaking strength of the incision wound increased significantly in all three extracts – water, alcohol, and Methanol ether. On the seventeenth day after the wounding, the excision wound model demonstrated a noteworthy rise in scar formation and wound constriction due to water extract [57].

Anticancer Activity

In vitro studies of *B. pinnatum* leaf crude extracts and its specific chromatographic fractions demonstrated growth inhibitory activity against human cervical cancer cells. The leaf extract and its fraction F4 (Petroleum Ether: Ethyl Acetate, 50:50) exhibited dose-dependent cytotoxic activity. Additionally, the inhibition of viral transcription of HPV18 was less in cells treated with fraction F4, indicating a higher concentration of active principles in this fraction.

Antioxidant Activity

The physiological burden of free radicals leads to an imbalance in the homeostatic process between oxidants and antioxidants in the body. This imbalance results in oxidative stress, which is believed to be a primary cause of aging and various human diseases, including arteriosclerosis, stroke, and diabetes. Morales and colleagues suggested that quercetin has a significant protective effect against cadmium-induced nephrotoxicity. This effect is attributed to an increase in Metallothionein, a small cysteine-rich protein, and the expression of eNOS (endothelial nitric oxide synthase). Additionally, quercetin inhibits the expression of COX-2 (cyclooxygenase-2) and iNOS (inducible nitric oxide synthase).

Anti-Inflammatory Activity

The leaf extracts of *B. pinnatum* – including pet-ether, chloroform, acetone, methanol, aqueous, alkaloidal fraction, flavonoid fraction, phenol, phenolic acid, and alkaloidal anhydride – demonstrated anti-inflammatory activity. This was observed at a dose of 500 mg/kg, administered orally once a day for two days, in the Formaldehyde-induced hind paw edema model in rats. The methanolic fraction of *B. pinnatum* showed a noticeable inhibition of formaldehyde-induced edema during the early phases, with significant inhibition in the later phases, when compared to the standard drug, Indomethacin [58].

Anti-ulcer Activity

It also been demonstrated by the investigators that the Methanol-soluble fraction of *B. pinnatum* leaf extract inhibited the development of a variety of acute ulcers induced in the stomach and duodenum of rats and guinea pigs.

Hepatoprotective Activity

The aqueous and ethanolic extracts of *B. pinnatum* demonstrated hepatoprotective activity at doses of 250 and 500 mg/kg, administered orally, in rats with N-diethyl nitrosamine (DENA)-induced hepatic injury. At the 500 mg/kg dose, the ethanolic extract provided slight protection to the liver. The aqueous extract of *B. pinnatum* at both doses (250 and 500 mg/kg) showed significant liver protection against DENA-induced liver toxicity.

CONCLUSIONS

B. pinnatum is a very common herbal plant and it is used in the treatment of many disorders, such as gastrointestinal discomfort, respiratory diseases, skin diseases etc. It contains various phytoconstituents which are mainly responsible for therapeutic action. The sight of the present study investigation was executed to collate the anti-obesity action of Euphorbia hirta. This study also includes the traditional as well as pharmacological uses of *B.pinnatum* with scientific evidences.

REFERENCES

1. Fruh SM, Graves RJ, Hauff C, Williams SG, Hall HR. Weight bias and stigma: Impact on health. Nurs Clin North Am. 2021;56(4):479–493. doi: 10.1016/j.cnur.2021.07.001.
2. Nam GE, Kim YH, Han K, Jung JH, Rhee EJ, Lee WY. Obesity fact sheet in Korea, 2020: Prevalence of obesity by obesity class from 2009 to 2018. J Obes Metab Syndr. 2021;30(2):141. doi: 10.7570/jomes21056.
3. Seo MH, Lee WY, Kim SS, Kang JH, Kang JH, Kim KK, et al. 2018 Korean society for the study of obesity guideline for the management of obesity in Korea. J Obes Metab Syndr. 2019;28(1):40–45. doi: 10.7570/jomes.2019.28.1.40.
4. Telci Caklili O, Cesur M, Mikhailidis DP, Rizzo M. Novel anti-obesity therapies and their different effects and safety profiles: A critical overview. Diabetes Metab Syndr Obes. 2023;16:1767–1774. doi: 10.2147/DMSO.S392684.
5. Kapoor N, Kalra S, Al Mahmeed W, Al-Rasadi K, Al-Alawi K, Banach M, et al. The dual pandemics of COVID-19 and obesity: Bidirectional impact. Diabetes Ther. 2022;13(10):1723–1736. doi: 10.1007/s13300-022-01311-2.
6. World Health Organization. Constitution of the world health organization.
7. Swinburn BA, Kraak VI, Allender S, Atkins VJ, Baker PI, Bogard JR, et al. The global syndemic of obesity, undernutrition, and climate change: The Lancet Commission report. Lancet. 2019;393(10173):791–846. doi: 10.1016/S0140-6736(18)32822-8.
8. Nihalani N, Schwartz TL, Siddiqui UA, Megna JL. Weight gain, obesity, and psychotropic prescribing. J Obes. 2011;2011(1):893629. doi: 10.1155/2011/893629.
9. Cappuccio FP, Taggart FM, Kandala NB, Currie A, Peile E, Stranges S, et al. Meta-analysis of short sleep duration and obesity in children and adults. Sleep. 2008;31(5):619–626. doi: 10.1093/sleep/31.5.619.
10. Noh J. The effect of circadian and sleep disruptions on obesity risk. J Obes Metab Syndr. 2018;27(2):78–83. doi: 10.7570/jomes.2018.27.2.78.
11. McAllister EJ, Dhurandhar NV, Keith SW, Aronne LJ, Barger J, Baskin M, et al. Ten putative contributors to the obesity epidemic. Crit Rev Food Sci Nutr. 2009;49(10):868–913. doi: 10.1080/10408390903372599.
12. Lim HJ, Xue H, Wang Y. Global trends in obesity. In: Handbook of Eating and Drinking: Interdisciplinary Perspectives. 2020:1217–1235.
13. Bray GA, Kim KK, Wilding JP, World Obesity Federation. Obesity: A chronic relapsing progressive disease process. A position statement of the World Obesity Federation. Obes Rev. 2017;18(7):715–723. doi: 10.1111/obr.12551.
14. Burki T. European Commission classifies obesity as a chronic disease. Lancet Diabetes Endocrinol. 2021;9(7):418. doi: 10.1016/S2213-8587(21)00145-5.
15. Rubino F, Batterham RL, Koch M, Mingrone G, le Roux CW, Farooqi IS, et al. Lancet Diabetes & Endocrinology Commission on the definition and diagnosis of clinical obesity. Lancet Diabetes Endocrinol. 2023;11(4):226–228. doi: 10.1016/S2213-8587(23)00058-X.
16. Hall KD, Kahan S. Maintenance of lost weight and long-term management of obesity. Med Clin North Am. 2018;102(1):183–197. doi: 10.1016/j.mcna.2017.08.012.
17. Look AHEAD Research Group Wing RR, Bolin P, Brancati FL, Bray GA, Clark JM, et al. Cardiovascular effects of intensive lifestyle intervention in type 2 diabetes. N Engl J Med. 2013;369(2):145–154. doi: 10.1056/NEJMoa1212914.
18. Elhayany A, Lustman A, Abel R, Attal-Singer J, Vinker S. A low carbohydrate Mediterranean diet improves cardiovascular risk factors and diabetes control among overweight patients with

type 2 diabetes mellitus: A 1-year prospective randomized intervention study. Diabetes Obes Metab. 2010;12(3):204–209. doi: 10.1111/j.1463-1326.2009.01151.x.
19. Harrington J, Felker GM, Januzzi JL, Lam CS, Lingvay I, Pagidipati NJ, et al. Worth their weight? An update on new and emerging pharmacologic agents for obesity and their potential role for persons with cardiac conditions. Current Cardiol Rep. 2024;26(3):61–71. doi: 10.1007/s11886-023-02016-z.
20. Green L, Taddei-Allen P. Shifting paradigms: Reframing coverage of antiobesity medications for plan sponsors. J Manag Care Spec Pharm. 2023;29(5):564–568. doi: 10.18553/jmcp.2023.29.5.564.
21. Gadde KM, Atkins KD. The limits and challenges of antiobesity pharmacotherapy. Expert Opin Pharmacother. 2020;21(11):1319–1328. doi: 10.1080/14656566.2020.1748599.
22. Li RY, Song HD, Shi WJ, Hu SM, Yang YS, Tang JF, et al. Galanin inhibits leptin expression and secretion in rat adipose tissue and 3T3-L1 adipocytes. J Mol Endocrinol. 2004;33(1):11–20. doi: 10.1677/jme.0.0330011.
23. Collaborators GB, Ärnlöv J. Global burden of 87 risk factors in 204 countries and territories, 1990–2019: A systematic analysis for the Global Burden of Disease Study 2019. Lancet. 2020;396(10258):1223–1249. doi: 10.1016/S0140-6736(20)30752-2.
24. Okunogbe A, Nugent R, Spencer G, Powis J, Ralston J, Wilding J. Economic impacts of overweight and obesity: Current and future estimates for 161 countries. BMJ Glob Health. 2022;7(9):e009773. doi: 10.1136/bmjgh-2022-009773.
25. Field AE, Coakley EH, Must A, Spadano JL, Laird N, Dietz WH, et al. Impact of overweight on the risk of developing common chronic diseases during a 10-year period. Arch Intern Med. 2001;161(13):1581–1586. doi: 10.1001/archinte.161.13.1581.
26. Flier JS. Obesity wars: Molecular progress confronts an expanding epidemic. Cell. 2004;116(2):337–350. doi: 10.1016/s0092-8674(03)01081-x.
27. Moro CO, Basile G. Obesity and medicinal plants. Fitoterapia. 2000;71 Suppl 1:S73–S82. doi: 10.1016/s0367-326x(00)00177-5.
28. Lee JS, Lee MK, Ha TY, Bok SH, Park HM, Jeong KS, et al. Supplementation of whole persimmon leaf improves lipid profiles and suppresses body weight gain in rats fed high-fat diet. Food Chem Toxicol. 2006;44(11):1875–1883. doi: 10.1016/j.fct.2006.06.014.
29. Nagaratna A, Hegde PL. A comprehensive review on Parnabeeja [Bryophyllum pinnatum (Lam.) Oken]. J Med Plants Stud. 2015;3(5):166–171.
30. Beshir SA, Elnour AA, Soorya A, Mohamed AP, Goh SS, Hussain N, et al. A narrative review of approved and emerging anti-obesity medications. Saudi Pharm J. 2023;31(10):101757. doi: 10.1016/j.jsps.2023.101757.
31. Kishino E, Ito T, Fujita K, Kiuchi Y. A mixture of the Salacia retuculata (Kotalahimbutu) aqueous extract and cyclodextrin reduces the accumulation of visceral fat mass in mice and rats with high-fat diet induced obesity. J Nutr. 2006;136(2): 433–439. doi: 10.1093/jn/136.2.433.
32. Shrestha S, Bhattarai BR, Lee KH, Cho H. Mono-and disalicylic acid derivatives: PTP1B inhibitors as potential anti-obesity drugs. Bioorg Med Chem. 2007;15(20):6535–6548. doi: 10.1016/j.bmc.2007.07.010.
33. Barness LA, Opitz JM, Gilbert-Barness E. Obesity: Genetic, molecular, and environmental aspects. Am J Med Genet A. 2007;143(24):3016–3034. doi: 10.1002/ajmg.a.32035.
34. Afzal M, Ahmad K, Saleem S, Kazmi I, Anwar F. Effect of Bryophyllum pinnatum Lam. on N-diethyl nitrosamine induced hepatic injury in rats. Biosci Biotechnol Res Asia. 2016;9(2). doi: 10.13005/bbra/1060.
35. Kamboj A, Saluja A. Bryophyllum pinnatum (Lam.) Kurz.: Phytochemical and pharmacological profile: A review. Pharmacognosy Reviews. 2009;3(6):364.
36. Pal S, Chaudhuri AN. Studies on the anti-ulcer activity of a Bryophyllum pinnatum leaf extract in experimental animals. J Ethnopharmacol. 1991;33(1–2):97–102. doi: 10.1016/0378-8741(91)90168-D.
37. Igwe SA, Akunyili DN. Analgesic effects of aqueous extracts of the leaves of Bryophyllum pinnatum. Pharma Biol. 2005;43(8):658–661. doi: 10.1080/13880200500383108.

38. Pal S, Sen T, Chaudhuri AK. Neuropsychopharmacological profile of the methanolic fraction of Bryophyllum pinnatum leaf extract. J Pharm Pharmacol. 1999;51(3):313–318. doi: 10.1211/0022357991772312.
39. Jaiswal S, Sawhney S. Correlation of epiphyllous bud differentiation with foliar senescence in crassulacean succulent Kalanchoe pinnata as revealed by thidiazuron and ethrel application. J Plant Physiol. 2006;163(7):717–722. doi: 10.1016/j.jplph.2005.08.001.
40. Akinpelu DA. Antimicrobial activity of Bryophyllum pinnatum leaves. Fitoterapia. 2000;71(2):193–194. doi: 10.1016/s0367-326x(99)00135-5.
41. Okwu DE, Nnamdi FU. Two novel flavonoids from Bryophyllum pinnatum and their antimicrobial activity. J Chem Pharm Res. 2011;3(2):1–10.
42. Aransiola EF, Daramola MO, Iwalewa EO, Seluwa AM, Olufowobi OO. Anti-diabetic effect of Bryophyllum pinnatum leaves. IJBB. 2014;8(1):89–93.
43. Khan M, Patil PA, Shobha JC. Influence of Bryophyllum pinnatum (Lim.) leaf extract on wound healing in albino rats. J Nat Remedies. 2004;4(1):41–46. doi: 10.18311/jnr/2004/380.
44. Gesta S, Tseng YH, Kahn CR. Developmental origin of fat: Tracking obesity to its source. Cell. 2007;131(2):242–256. doi: 10.1016/j.cell.2007.10.004.
45. Balistreri CR, Caruso C, Candore G. The role of adipose tissue and adipokines in obesity-related inflammatory diseases. Mediators Inflamm. 2010;2010(1):802078. doi: 10.1155/2010/802078.
46. Patel PS, Buras ED, Balasubramanyam A. The role of the immune system in obesity and insulin resistance. J Obes. 2013;2013(1):616193. doi: 10.1155/2013/616193.
47. Kosteli A, Sugaru E, Haemmerle G, Martin JF, Lei J, Zechner R, et al. Weight loss and lipolysis promote a dynamic immune response in murine adipose tissue. J Clin Invest. 2010;120(10):3466–3479. doi: 10.1172/JCI42845.
48. Hotamisligil GS, Arner P, Caro JF, Atkinson RL, Spiegelman BM. Increased adipose tissue expression of tumor necrosis factor-alpha in human obesity and insulin resistance. J Clin Invest. 1995;95(5):2409–2415. doi: 10.1172/JCI117936.
49. Tsigos C, Kyrou I, Chala E, Tsapogas P, Stavridis JC, Raptis SA, et al. Circulating tumor necrosis factor alpha concentrations are higher in abdominal versus peripheral obesity. Metabolism. 1999;48(10):1332–1335. doi: 10.1016/s0026-0495(99)90277-9.
50. Fernández-Sánchez A, Madrigal-Santillán E, Bautista M, Esquivel-Soto J, Morales-González Á, Esquivel-Chirino C, et al. Inflammation, oxidative stress, and obesity. Int J Mol Sci. 2011;12(5):3117–3132. doi: 10.3390/ijms12053117.
51. Gahlaut A, Pawar SD, Mandal TK, Dabur R. Evaluation of clinical efficacy of Bryophyllum pinnatum Salisb for treatment of lithiasis. Int J Pharm Pharm Sci. 2012;4(4):505–507.
52. Gupta R, Lohani M, Arora S. Anti-inflammatory activity of the leaf extracts/fractions of Bryophyllum pinnatum Saliv. Syn. Int J Pharm Sci Rev Res. 2010;3(1):16–18.
53. Mahata S, Maru S, Shukla S, Pandey A, Mugesh G, Das BC, et al. Anticancer property of Bryophyllum pinnata (Lam.) Oken. leaf on human cervical cancer cells. BMC Complement Altern Med. 2012;12:15. doi: 10.1186/1472-6882-12-15.
54. Bagul M, Srinivasa H, Anandjiwala S, Rajani M. Phytochemical evaluation and free radical scavenging activity of Nagakesara (stamen of Mesua ferrea Linn. var. ferrea). Indian Drugs. 2006;43(8):665–670.
55. Harlalka GV, Patil CR, Patil MR. Protective effect of Kalanchoe pinnata pers.(Crassulaceae) on gentamicin-induced nephrotoxicity in rats. Indian J Pharmacol. 2007;39(4):201–205. doi: 10.4103/0253-7613.36540.
56. Sreejayan, Rao MN. Nitric oxide scavenging by curcuminoids. J Pharm Pharmacol. 1997;49(1):105–107. doi: 10.1111/j.2042-7158.1997.tb06761.x.
57. Jain VC, Patel NMb, Shah DP, Patel PK, Joshi BH. Antioxidant and antimicrobial activities of Bryophyllum calycinum salisb leaf. Pharmacologyonline. 2010;1:393–405.
58. Muzitano MF, Tinoco LW, Guette C, Kaiser CR, Rossi-Bergmann B, Costa SS. The antileishmanial activity assessment of unusual flavonoids from Kalanchoe pinnata. Phytochemistry. 2006;67(18):2071–2077. doi: 10.1016/j.phytochem.2006.06.027.

