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Hop Shoots (*Humulus lupulus*): Emerging Bioactive Components, Functional Properties, and Opportunities for Food and Bio-Industrial Applications

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ABSTRACT

The common hop (*Humulus lupulus L.*) is a dioecious perennial climbing plant and is referred to as a member of the Cannabaceae family, and is located in the northern temperate regions. Female plants are grown solely due to the large quantities of constituents they possess, which are primarily bitter principles and essential oils that are not only used in the industry but are also used as medicinal products. It is endowed with bioactive properties, including prenylated flavonoids, bitter and phenolic acids, terpenoids, and vitamins, antimicrobial, anti-inflammatory, antioxidant, estrogenic, neuroprotective, and hormonal modulation properties. The hop shoots contain the optimal composition of any micronutrient that is not caloric and thus can be added to health-promoting meals. They have a niche potential to produce and market because of their high market value, thus the high economic importance they have in the European market; the agro-climatic conditions of the regions in northern Pakistan create the possibility of the renewal of rural development. This paper intends to provide an overview of its novel bioactive compounds, properties, and food and biotechnological uses. A multidisciplinary approach to the application of the idea of harnessing the full potential of hop shoots will entail the use of both agricultural science, food technology, and pharmacology, as well as implementing it in the market preparation.

INTRODUCTION

The hop plant (*Humulus lupulus L.*) is a dioecious perennial climbing species of the Cannabaceae family, having historically been grown to be used as female inflorescences of the plant commonly referred to as cones or strobiles, which have achieved considerable success in the brewing industry because of its aromatic, bittering, and preservative qualities (Figure 1) [1]. However, among the cones, it possesses the beams of tenderness, young shoots every year sprouting out of the perennial rhizomes. They have even been called the vegetable so much desired by the Europeans in their cuisine, the most expensive vegetable in the world, and called simply the hop shoot in virtue of the subtle asparagus flavor, short growing season, scarcity [2]. They appeared in the pharmacopoeias of European pharmaceutical collections and folk medicine of the Middle Ages and were said to act on digestion, skin, and

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blood purification [3]. In recent decades, hop shoots have been receiving renewed attention due to renewed interest in functional foods and niche crops with high value. The scientific advances have enhanced the degree of knowledge with regard to the phytochemical composition of hop shoots. The previously described cone-related compounds (alpha -acids (humulones), 2 -acids (lupulones), xanthohumol, desmethylxanthohumol, and 8 -prenylnaringenin) also occur in shoots with varying concentrations [4]. They are metabolites, and they have diverse biological activities, including antimicrobial, antioxidant, anti-inflammatory, estrogenic, and anticancer activities [5-7]. The hop shoot is a functioning food with high amounts of vitamin C (as much as 40mg/100g), dietary fiber, essential minerals, and very small amounts of oxalic acid (less than 67mg/100g), making the Hop Shoot a food item as well as a culinary delight [8]. With the propagation of hop growers to every corner of the world, the hop shoots have drawn a lot of agricultural research. The interested areas, such as the Mediterranean Europe, which are interested in commercial production of hops due to the limitation of the photo period and the climate, are now wondering about the dual use of the cones and shoots production [9]. Pakistan has virtually no experience of hop cultivation and hop shoot production. However, the variation in agro-ecological conditions (diverse agro-ecological conditions), i.e., the temperate valleys of Gilgit-Baltistan, the elevated regions of Khyber Pakhtunkhwa, and the irrigated plains of the northern part of the Punjab, would support the growth of hop in case of the introduction of hop-photoperiod-adapted varieties. The main aim of the present review was to conduct a representative study regarding the new bioactive components, functions, and opportunities of food and bio-industrial exploitation of hop shoots. This review highlights the potential and the unfulfilled potential of hop shoot production in Pakistan and in the Pakistani agro-climatic regions, the opportunities, challenges, and research opportunities in the future.

Figure 1: *Humulus lupulus L.* Cones

Biologically Active Compounds

Hop shoots (*Humulus lupulus L.*) are biochemically rich vegetation since secondary metabolites are complex, and a great number of them are concentrated in the hop cones, but also in the young aerial shoots. These compounds belong to various chemical families, which are bitter acids, pre-phenylated flavonoids, volatile essential oils, phenolic acids, and other polyphenols [10]. The best concentrations of the compounds in the hop extracts were catechin and xanthohumol, with the level of the compounds being 1.22mg per gram to 2.70mg per gram and 1.09mg per gram to 2.67mg per gram, respectively. The concentrations of Rutin and chlorogenic acid were found to be 0.612-0.877 mg g -1, and the p-hydroxybenzoic acid, protocatechuic acid, syringic acid, and ellagic acid were 0.262-0.654 mg g -1. Epigallocatechin, p-coumaric, caffeic, and ferulic acids were also found in small amounts and at varying levels depending on the extraction mode, which is taken [11]. Future research opportunities, challenges, and directions.

Bitter Acids

Bitter acids are a hallmark of the *Humulus* genus and represent one of its most pharmacologically relevant phytochemical groups. They are classified into two structurally related subclasses: α-acids, also known as humulones, and β-acids, known as lupulones (Figure 2).

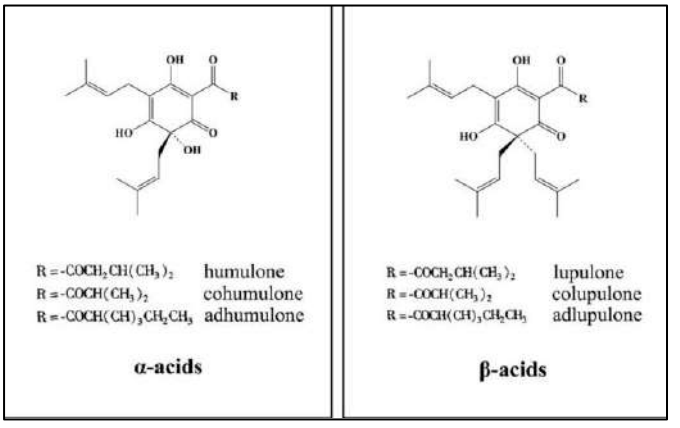

Figure 2: α-acids and β-acids of Humulus Genus

Both have a comparable acylphloroglucinol backbone and differ in prenylation patterns, which give different physicochemical properties and biological activities. The 1,5-acids, such as humulone, cohumulone, and adhumulone, are biosynthesized in hop tissues in the glandular trichomes of the branched-chain amino acid precursors by the action of the enzyme valerophenone synthase, and then by successive prenylations by prenyltransferases [12]. The 2 -acids such as lupulone, colupulone, and adlupulone are more hydrophobic than their 2 -acid analogues and exhibit strong antifungal effects due to their ability to disrupt ergosterol production in fungal membranes. In addition to antimicrobial

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activities, β-acids have also exhibited selective cytotoxicity in some cancer cell lines, which indicates that they can be used in cancer chemoprevention [13].

Prenylated Flavonoids

Prenylated flavonoids are also another important bioactive in the hops shoots and contribute to the hop shoot pharmacology and possible health applications as functional foods. Among them, the prenylated chalcone xanthohumol is the best-researched. The amounts of hop shoots, which, though lower than those of cones, are calculable, are also in their biological characteristics. Having diverse bioactivity, xanthohumol has been identified to exhibit antiproliferative, antioxidant, and anti-inflammatory properties on a diverse array of cancer cell lines, as well as inhibiting lipid peroxidation and inducible nitric oxide synthase (iNOS) and COX-2 expression [14]. The other prenylated chalcone identified in hop shoots is desmethylxanthohumol, which serves as a biosynthetic precursor to xanthohumol and the phytoestrogen 8-prenylnaringenin. The conversion can either occur enzymatically in the plant or in the metabolic conversion of the human gut microbiota. Of particular interest is one of the prenylated flavanones, 8-prenylnaringenin, which, in addition, is one of the strongest plant estrogens, being 100-fold weaker than genistein, the well-known soy isoflavone. They are prescribed to alleviate menopausal symptoms, osteoporosis prevention, and treatment of physiological functions that are dependent on hormones [15].

Essential Oils (*Volatile Terpenoids*)

Although the essential oil fraction of hop shoots is less compared to mature cones, it retains a typical blend of monoterpenes and sesquiterpenes, which can be found in aroma and bioactivity, and 2-myrcene is prevalent, which has anti-inflammatory, analgesic, and muscle-relaxant effects. The other monoterpenes are alpha pinene and limonene that were reported to possess anti-microbial and anti-inflammatory properties. Short-chain sesquiterpenes, which are selective agonists of the cannabinoid receptor CB2 (alpha-humulene, 2-caryophyllene, 2-farnesene), are also non-psychoactive and exhibit anti-inflammatory properties in addition to analgesic properties [16].

Phenolic Acids and Other Polyphenols

The phenolic acids are also very significant in the antioxidant properties of the hop shoots. Other typical ones are p-Coumaric, ferulic, and caffeic acids, which are low-density lipoproteins (LDL) oxidation inhibitors and free radical scavengers [17]. The other effects of the compounds include the protection of the vascular endothelium that could be translated into cardiovascular effects. The other polyphenols, such as flavonols and flavan-3-ols, are also biologically favourable to the human organism since they enhance the anti-inflammatory and vascular protective properties of hop shoots [18].

Minor Bioactive Constituents

The minor constituents of hop shoots along with the major bioactive groups, can make contributions to the functional properties of this group. These include amino acids and small peptides that have the potential of antioxidants or antimicrobial activity and traces of saponins. They have not been fully studied as to their pharmacological usefulness in the hop shoots, although are a hopeful research potential in the future [19].

Biological Activities of Hop Shoots (*Humulus lupulus*)

The principal classes of bioactive compounds present in hop shoots (*Humulus lupulus*), their model molecules, and the biological effects that they have are outlined (Table 1).

Table 1: Major Biologically Active Compounds in Hop Shoots and Their Biological Activities

Compound Class	Representative Compounds	Chemical Nature	Major Biological Activities	References
Bitter Acids (α-acids)	Humulone, Cohumulone, Adhumulone	Acylphloroglucinol derivatives	Antioxidant, Antibacterial against Gram-positive bacteria, anti-inflammatory	[20]
Bitter Acids (β-acids)	Lupulone, Colupulone, Adlupulone	Acylphloroglucinol derivatives	Antifungal, antimicrobial synergy, and selective cytotoxicity in cancer cells	[21]
Prenylated Flavonoids	Xanthohumol	Prenylated chalcone	Anticancer, antioxidant, anti-inflammatory, chemopreventive	[22]
	Desmethylxanthohumol	Prenylated chalcone	COVID-19, Precursor to phytoestrogen 8-prenylnaringenin	[23]
	8-Prenylnaringenin	Prenylated flavanone	Potent estrogenic activity, relief of menopausal symptoms, bone health	[24]
Essential Oils	β-Myrcene, α-Humulene, β-Caryophyllene, β-Farnesene	Mono-/sesquiterpene hydrocarbons	Anti-inflammatory, analgesic, antimicrobial, sedative	[25]
Phenolic Acids	p-Coumaric, Ferulic, Caffeic acids	Hydroxycinnamic acids	Antioxidant, cardiovascular protection	[26]
Other Polyphenols	Quercetin Derivatives, Catechins	Flavonols, flavan-3-ols	Anti-inflammatory, antioxidant, vascular protection	[27]

In recent years, the biological functions of hops have been the subject of multiple investigations. The biological activities of hops include anti-inflammatory, anticancer, anti-Alzheimer, antiviral, antidiabetic, antimicrobial, and antifungal activities. The possible therapeutic uses of hop bioactive components in the management of human illnesses are given (Figure 3) [25].

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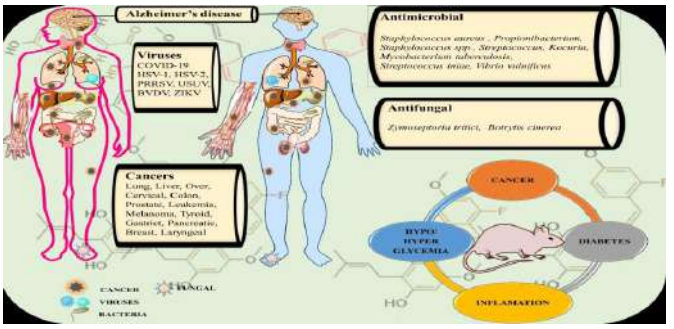

Figure 3: Overview of the components of hop shoots in related human diseases

Antimicrobial Activity

Hop-derived bitter acids, particularly α- and β-acids, have well-documented antibacterial and antifungal properties. In shoots, these compounds have been shown to inhibit gram-positive bacteria such as *Staphylococcus aureus* and *Listeria monocytogenes* by disrupting cytoplasmic membranes and inhibiting key metabolic enzymes. β-acids also display potent antifungal effects, interfering with ergosterol biosynthesis and fungal membrane stability. Some studies suggest that combining hop extracts with antibiotics can reduce bacterial resistance, offering potential in antimicrobial stewardship [26].

Antifungal Activity

Numerous investigations have demonstrated the antifungal action of prenylflavonoids. For illustration, cohumulone and desmethylxanthohumol (DXN) demonstrated antifungal activity against Zymoseptoria tritici with half-maximum inhibitory doses of 0.11 and 0.2 g/L, respectively. 88 With an EC50 value of 4.32 µg/mL, it was shown that iso-xanthohumol (IXN) drastically reduced antifungal activity against B. cinerea. This study demonstrates that phytopathogenic fungi can be treated with IXN [27].

Anti-inflammatory Effects

Some bioactive compounds in hop shoots, such as xanthohumol and alpha-humulene, have anti-inflammatory effects through the modulation of NF-κB signaling pathways and the downregulation of pro-inflammatory cytokines, TNF-alpha, and IL-1 beta. The sesquiterpene in hop oils, β-caryophyllene, acts on cannabinoid CB2 receptors and decreases inflammation without having a psychoactive effect. The properties have potential consequences in treating inflammatory diseases, including arthritis and metabolic inflammation [28].

Antioxidant Potential

Hop shoots are rich in phenolic acids (caffeic and ferulic) and flavonoids (quercetin derivatives) that exert high antioxidant capacity through reactive oxygen species (ROS) scavenging, lipid peroxidation inhibition, and up-regulation of endogenous antioxidant enzyme activities. This antioxidative activity is important in the prevention of oxidative stress-based pathology like cardiovascular disease, neurodegeneration, or some cancers [29].

Actions: Estrogenic, Hormone-Modulating

Hop shoots include 8-prenylnaringenin, which is one of the strongest phytoestrogens in the natural world. This compound acts on estrogen receptors, alpha and beta, and has the potential to provide a therapeutic benefit to menopausal symptom relief, prevention of osteoporosis, and hormone-related metabolic health [30]. It should be applied in a controlled manner because it is highly potent.

Neuroprotective Properties

Preclinical evidence indicates that prenylated flavonoids in hops could be neuroprotective owing to their antioxidant activity, neurotransmitter systems regulation, and anti-inflammatory effects. This has a possibility of future usage in the treatment of neurodegenerative diseases like Alzheimer's and Parkinson's diseases, but studies on shoots are few compared to cones [31, 32].

Antiviral Covid-19

Since 2019, millions of people worldwide have contracted the coronavirus, often known as SARS-CoV-2 or COVID-19. Nevertheless, hop illnesses were induced by the detected hop stunt viroid (HSVd), apple fruit crinkle viroid (AFCVd), citrus bark cracking viroid (CBCVd), and hop latent viroid (HLVd). Lin et al. showed that xanthohumol was a pan-inhibitor of the primary protease of COVID-19, with an IC50 value of 1.53 µM [33].

Anticancer activity

Numerous studies reported that xanthohumol (XN) from hop shoots induced cancer cell death and inhibited tumor growth *in vitro* and *in vivo*. The effect of xanthohumol was shown in various human cancers, such as estrogen receptor-positive breast cancer cells (MCF-7), ovarian (A2780), colon (HT-29), cervical cancer, melanoma, hepatocellular, and prostate (DU145, PC-3), and lung cancer [34].

Cardiovascular Impacts

Hops are typically extracted using any organic solvent or supercritical CO_2. The extractable hop resins and essential oils make up most of the hop extract, whereas cellulose and residual polar compounds make up the spent hop. A wide range of polyphenols can be obtained by extracting the wasted hop extract using either water or ethanol/water. The inhibition of ADP-induced platelet aggregation by the wasted hop extract may be advantageous for the control of platelet and endothelial function [35].

Metabolic Health Benefits

Some of the hop polyphenols affect glucose and lipid metabolism. It has also been demonstrated that xanthohumol (XN) enhances insulin sensitivity and

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decreases adipogenesis and plasma triglycerides in animal models. These effects suggest that hop shoot extracts may have a role in the prevention of metabolic syndrome and weight management programs. Humulone and lupulone are bitter acids that have antibacterial and antifungal effects, alter microbial membranes, and interfere with the synthesis of ergosterol. Prenylated flavonoids and terpenes, such as xanthohumol, alpha-humulene, and beta-caryophyllene, have shown anti-inflammatory action [24]. Other positive effects are neuroprotective and metabolic, which means that hop shoots are broadly therapeutic (Table 2).

Table 2: Biological Activities of Hop Shoot Compounds and Their Mechanisms of Action

Biological Activity	Key Compounds	Mechanism of Action	References
Antibacterial	Humulone, Lupulone	Disrupts bacterial membranes, inhibits enzymatic activity	[26]
Antifungal	Lupulone, Colupulone	Interferes with ergosterol synthesis, damages fungal cell membranes	[27]
Anti-inflammatory	Xanthohumol (XN) α-Humulene, β-Caryophyllene	Inhibits NF-κB signaling, reduces TNF-α, and IL-1β activates CB2 receptors	[28]
Antioxidant	Caffeic acid, Ferulic acid, Quercetin	Scavenges ROS, inhibits lipid peroxidation, and enhances antioxidant enzymes	[29]
Estrogenic Activity	8-Prenylnaringenin	Binds estrogen receptors α/β, modulates hormonal activity	[30]
Neuroprotective	Xanthohumol, Quercetin	Reduces oxidative damage, modulates neurotransmission, and inhibits neuroinflammation	[31, 32]
Metabolic Regulation	Xanthohumol	Improves insulin sensitivity, reduces adipogenesis, and lowers plasma triglycerides	[33]

Nutritional Composition and Functional Potential of Hop Shoots

Hop shoots (*Humulus lupulus*) are not only a source of pharmacologically active phytochemicals but also contain essential nutrients that contribute to their functional food value. Although much of the research has focused on the phytochemical profile of hop cones, recent analyses indicate that young shoots also possess a balanced composition of macronutrients, micronutrients, and bioactive non-nutrient compounds. This composition underpins their potential as a seasonal delicacy in gourmet cuisine and as a candidate for inclusion in functional foods.

Macronutrient Profile

The fresh hop shoots consist mostly of water (about 85-90%), and the levels of calories are low; thereby, they can be used in weight-conscious diets. Carbs are moderate, primarily consisting of dietary fiber, which helps gut health and contributes to the health of microbiota in the gut. The range of proteins is 2-3/100g fresh weight, which supplies essential amino acids in moderate amounts. There is also a small amount of lipids and a healthy percentage of polyunsaturated to saturated fatty acids that are beneficial to cardiovascular health [36].

Micronutrients

Hop shoots contain many vitamins, especially vitamin C, vitamin E, and some vitamins of the B-complex (folate, niacin). These play a role in antioxidant defense and metabolic roles. Analysis of the minerals has portrayed significant concentrations of potassium, calcium, magnesium, and traces of iron and zinc, which are vital in enzyme processes as well as bone conditions [37].

Fiber and Prebiotic Potential

The cellulose, hemicellulose, and pectin dietary fiber in hop shoots maintain intestinal motility and can have prebiotic activity by increasing the growth of helpful gut bacteria. This, together with their polyphenol content, could synergistically stimulate gut health, though little clinical evidence exists [36].

Nutritional and Culinary Relevance in Pakistan

In select regions of Europe, the hop shoots are regarded as a luxurious seasonal crop; there is little practice and consumption of these in Pakistan. The diverse agro-climate conditions in the country can, however, accommodate the cultivation of hops, especially in the cooler areas. The nutritional profile of hop shoots shows low-calorie, high-moisture food having moderate protein and dietary fiber content (Table 3). They contain the necessary vitamins, which include vitamin C and vitamin E, and the B-complex vitamin including folate. The minerals present are potassium, calcium, magnesium, iron, and zinc, which serve cardiovascular, bone, enzymatic systems, and immunity [37].

Table 3: Nutritional Composition of Hop Shoots (per 100 g Fresh Weight)

Component	Content Range	Nutritional Relevance	References
Water (%)	85–90	Hydration, low energy density	[36]
Energy (kcal)	30–45	Low-calorie seasonal vegetable	[36]
Protein (g)	2–3	Moderate amino acid contribution	[36]
Total fat (g)	0.3–0.6	Minimal fat, favorable PUFA:SFA ratio	[36]
Carbohydrates (g)	5–7	Includes dietary fiber	[36]

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Fiber (g)	2–3	Gastrointestinal health, prebiotic potential	[36]
Vitamin C (mg)	25–35	Antioxidant, immune support	[36]
Vitamin E (mg)	0.8–1.2	Lipid antioxidant, skin health	[36]
Folate (µg)	50–70	DNA synthesis, pregnancy health	[36]
Potassium (mg)	350–450	Blood pressure regulation	[36]
Calcium (mg)	25–40	Bone and dental health	[36]
Magnesium (mg)	15–25	Enzyme function, muscle relaxation	[36]
Iron (mg)	0.8–1.2	Hemoglobin synthesis	[36]
Zinc (mg)	0.2–0.4	Immune support, wound healing	[36]

Agronomic and Economic Potential of Hop Shoots

Hop shoots are the costliest vegetables in the world and retail from 1,000 to 1,200 euros per kilogram in seasonal European markets [38]. This is because of their labor-intensive harvesting methods, limited seasonal supply, and their distinctive culinary qualities, which made them highly valued. Although the hop plants are traditionally planted with cones that are used in brewing, they can be controlled in a manner that generates edible cones that give the growers another source of revenue.

Cultivation Requirements

The temperature and cool climate would be of great importance in the cultivation of hops; the temperature should be between 16 and 24C of the soil and well-drained soils that are rich in nutrients. The harvesting of shoots is usually done in early spring as the shoots are 10-15 cm long before lignification's make them less tender. The plants are perennial, such that production of annual shoots is possible without replacing the plants. Organic matter fertilization, as well as sufficient irrigation, improves the quality of phytochemicals and yield [39].

Harvesting and Postharvest Handling

Hop shoot harvesting is also a laborious activity because it requires manual picking of young apical shoots, as well as lateral buds. The critical stages of preservation of sensory quality and nutritional value are quick postharvest cooling and gentle handling. Because of their fragility, the shoots are best eaten freshly, but when stored under controlled atmospheres, the shelf life of the produce can take up to one week [39].

Economic Viability and Potential Market

Hop shoots can be sold as high-end gourmet vegetables in Europe, which are frequently utilized in luxury restaurants. Their low quantity, coupled with their distinct taste and texture, enables them to be highly valued. To growers in countries where hop growing has already occurred, new income can be obtained by diversifying the production of shoots, but without a significant impact on the resulting cone production. The economic model is based on the balance between the labor cost and market demand [37].

Potential in Pakistan

The north and northwestern parts of Pakistan, including Gilgit-Baltistan, Swat, and parts of Khyber Pakhtunkhwa, have agro-climatic features such as temperate hop cultures. The introduction of hop shoots would open niche exports to the Gulf and European markets, and provide completely new, nutritious food to the local markets. Small-scale high-value horticultural businesses (hop shoots) would be helpful to rural populations and, therefore, women-organized agriculture. Nonetheless, issues like poor awareness, upfront cost of investments, and the necessity to employ skilled labor would need to be solved via agricultural extension modules and pilot farm projects. The agronomic and economic factors are several on which the production of the hop shoot is dependent since the crop thrives well in temperate to cool climates (16 24 o C) and in soils that are well drained and consist of high organic matter levels [40]. In Pakistan, northwestern areas like Gilgit-Baltistan and Swat have a good environment, which has potential opportunities for niche, high-value exports and income diversification of rural farmers (Table 4).

Table 4: Agronomic and economic considerations for hop shoot production

Parameter	Details	References
Climate requirement	Temperate to cool (16–24°C)	[37, 39]
Soil requirement	Well-drained, fertile, organic matter-rich	[37, 39]
Harvest time	Early spring, shoots 10–15 cm long	[37, 39]
Harvest method	Manual cutting of tender apical shoots and lateral buds	[37]
Postharvest handling	Rapid cooling, minimal handling, possible controlled-atmosphere storage	[37, 39]
Market price (Europe)	€1,000–€1,200/kg during season	[37, 39]
Potential regions in Pakistan	Gilgit-Baltistan, Swat, northern Khyber Pakhtunkhwa	[37]
Economic benefits	Diversification of farm income, high-value crop potential, niche export opportunities	[37, 39]

CONCLUSIONS

Hop shoots are a bioactive and highly nutritional vegetable, which has potential uses in gastronomy, medicine, and agribusiness. These various phytochemical compositions provide antibacterial, anti-inflammatory, antioxidant, estrogenic, metabolic, and neuroprotective properties, which underscore their use as a functional food ingredient.

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In addition, the fact that hop shoots have high market value will enable agricultural diversification of climatically favorable areas such as the north of Pakistan, because well-structured clinical experiments are needed to demonstrate the bioactivities of hop shoots, and improvements in crop production and after-harvesting. There is a strong need, therefore, to integrate work on agronomy, food science, and biomedical research, facilitating their productive and sustainable production, value-added use, and commercialization.

Authors Contribution

Conceptualization: MKS
Methodology: ZA, AA,
Formal analysis: STS, SS, NZ, AK, KS, IA
Writing and Drafting: AA
Review and Editing: MKS, STS, ZA, AA, SS, NZ, AK, KS, IA

All authors approved the final manuscript and take responsibility for the integrity of the work.

Conflicts of Interest

All the authors declare no conflict of interest.

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