

**TRADITIONAL USES, PHYTOCHEMISTRY AND
PHARMACOLOGICAL ACTIVITIES OF *Betula utilis***Santosh¹, Yogesh Kumar Sharma^{1*}, Abhishek Godara¹¹Department of Pharmacology, Jaipur College of Pharmacy, Jaipur, Rajasthan, India**ABSTRACT**

Plants offer a vast array of secondary metabolites with applications in preventing and treating diseases. This review explores the potential therapeutic benefits of *Betula utilis*, a medicinal plant native to the Himalayas. With over 250,000 plant species, more than a thousand have shown significant pharmacological properties. *Betula utilis*, known as Himalayan birch or bhojpatra, exhibits antimicrobial, anti-inflammatory, anticancer, antioxidant, and anti-HIV properties attributed to pentacyclic triterpenoids in its bark, including betulin and betulinic acid. These compounds play a crucial role in reducing triglyceride formation and inhibiting key enzymes like diacylglycerol acetyltransferase (DGAT) involved in obesity-related processes. Betulinic acid demonstrates pancreatic lipase inhibitory effects, decreasing fat absorption and contributing to weight loss. The plant's extracts exhibit antifungal, antibacterial, and anticancer activities, making them potential candidates for various therapeutic applications. The botanical description highlights *Betula utilis*' robust nature, thriving in challenging Himalayan environments. Traditional uses, such as crafting paper and treating urinary infections, emphasize its cultural significance. Chemical constituents like betulinic acid showcase a rich pharmacological profile, including anti-HIV effects. The bark's antioxidant properties, along with free radical scavenging and reducing activities, further contribute to its medicinal potential. This comprehensive exploration positions *Betula utilis* as a promising candidate for diverse medical applications, particularly in the context of anti-obesity interventions.

Keywords: *Betula utilis*, Anticancer, Antidiabetic, Traditional uses, Phytochemistry, etc.

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INTRODUCTION

Plants represent a valuable reservoir of diverse secondary metabolites, offering a myriad of applications for the prevention and treatment of various diseases [1]. These natural compounds, obtained directly or indirectly from plants, contribute significantly to the well-being of humans and animals [2]. While some drugs are directly derived from plants, others incorporate plant-derived materials. Despite the identification of numerous phytochemicals with various pharmacological actions, there is still a need to assess the phytochemical content and pharmacological actions of many medicinal plants for defining efficacy and safety. A substantial portion, more than 30%, of plant species has been utilized for medicinal purposes, particularly in developing countries like India and China, where plants contribute to nearly 80% of medicinal practices [3]. Medicinal plants are considered safe due to minimal side effects, making them suitable for use across diverse age groups and genders. In the realm of anti-obesity interventions, herbal remedies play a significant role. With over 250,000 plant species, more than a thousand have demonstrated significant pharmacological properties [4]. One such traditional medicinal plant is *Betula utilis* (Himalayan birch or bhojpatra), a birch tree indigenous to the Himalayas and known to thrive at elevations up to 4,500 m. *Betula utilis* exhibits various pharmacological activities, including antimicrobial, anti-inflammatory, anticancer, antioxidant, and anti-HIV properties. The bark of *Betula utilis* contains pentacyclic triterpenoids such as betulin, betulic acid, sitosterol, oleanolic acid, acetyloleanolic acid, lupeol, lupenone, methyl betulonate, methyl betulate, and a novel triterpenoid known as karachic acid [5]. Pentacyclic triterpenoids play a role in reducing triglyceride formation by inhibiting DGAT, an enzyme crucial for the final step of triglyceride synthesis (Chung et al., 2006). Betulinic acid, a constituent of *Betula utilis*, exhibits both anti-inflammatory and DGAT inhibitory properties. Additionally, it demonstrates pancreatic lipase inhibitory effects and induces adipocyte lipolysis. These compounds inhibit lipases from breaking down ingested fat into absorbable free fatty acids and monoglycerides, thereby reducing the overall absorption of ingested fat and leading to weight loss [6]. The modulation of fat and carbohydrate metabolism suggests the potential of *Betula utilis* as a lead for the treatment of obesity and associated disorders.

METHODOLOGY

A comprehensive literature review on *Betula utilis* was conducted, utilizing a variety of both online and offline resources. Primary data sources included research and review articles published by various reputable publishers such as Elsevier, PSCI, Springer, and JDDT. Online databases such as NEJM, Science Direct, PubMed, Sci-Hub, and Library Genesis were also

consulted for extensive information on *Betula utilis*. Additionally, various journals, book chapters, and web pages were explored to ensure a thorough collection of literature on *Betula utilis*. To affirm the significance of this plant in Ayurvedic, Unani, Siddha, and folk medicinal formulations, the Indian Medicinal Plant Database (NMPB), operated by the National Medicinal Plants Board, was referenced. The review provides fundamental insights into *Betula utilis*, presenting essential information along with recent advancements related to this plant.

Botanical description

Betula utilis, commonly known as bhojpatra in the Indian Himalaya, is a robust perennial plant of moderate size, reaching heights of up to 20 meters. It thrives in challenging environments, specifically along the Himalayan ranges from Bhutan westwards, thriving at altitudes of up to 4200 meters. The local name "bhojpatra" reflects its significance in the region.

Notably, the first high-altitude bhojpatra nursery was established in 1993 at Chirbasa, just above Gangotri. In India, *Betula utilis* is naturally found in Uttarakhand and the higher regions of U.P. [7]. In Uttarakhand, it specifically grows along moraines around Bhojbas, in close proximity to the snout of the Gangotri glacier [8].

Scientific Classification

Kingdom : *Plantae*
Phylum : *Tracheophyta*
Class : *Magnoliopsida*
Order : *Corylales*
Family : *Betulaceae*
Genus : *Betula*
Species : *utilis*

Betula utilis belongs to the family *Betulaceae* and exhibits distinctive characteristics in its native habitat. In its natural environment, *B. utilis* often forms forests, growing either as a shrub or a tree that can attain heights of up to 20 meters (66 feet) (Figure 1). Typically, it thrives amidst scattered conifers, accompanied by an undergrowth of shrubs, including evergreen *Rhododendron*. The growth pattern of this tree is influenced by the pressure exerted by deep winter snow in the Himalayas, often resulting in a bent form. The leaves of *Betula utilis* are ovate, measuring 5 to 10 cm (2.0 to 3.9 inches) in length, featuring serrated margins and a slight hairiness. The flowering period spans from May to July, characterized by a few male catkins and short, single (sometimes paired) female catkins. Male flowers possess a perianth with four parts, while female flowers lack a perianth. The fruits mature in September–October.

One distinctive feature is the thin, papery bark, which exhibits a shiny texture and can appear in shades of reddish-brown, reddish-white, or white. Horizontal lenticels are present on the bark. The bark has a unique characteristic of peeling off in broad, horizontal belts, making it particularly suitable for creating large, even pages for texts [9].



Figure 1 : Bark of *Betula utilis*

Traditional uses

The bark of the Himalayan birch, known as Bhûrja in Sanskrit, played a crucial role in ancient India where it was utilized for creating paper used in writing lengthy scriptures and texts, particularly in Sanskrit and other scripts. The term "bhûrja" in Sanskrit shares etymological roots with other Indo-European words, ultimately contributing to the common name "birch." Beyond its historical use in writing materials, the bark finds widespread applications, such as in packaging material and roof construction. Notably, the leaves of the Himalayan birch demonstrate efficacy in treating urinary tract infections, as well as issues related to the kidneys and bladder stones. The wood of the plant is employed in construction, while the foliage serves as fodder. However, the most prevalent use of the Himalayan birch is for firewood, leading to the elimination of extensive habitat areas. Additionally, various parts of the plant, including fungal growth known as "bhurjagranthi," have been integral components of local traditional medicine practices [10].

Chemical Constituents

The bark of *Betula utilis* is a rich source of various bioactive compounds, including but not limited to betulin, lupeol, oleanolic acid, acetyloheanolic acid, betulic acid, lupenone,

sitosterol, methyl betulonate, methyl betultriterpenoid, and karachic acid. *Betula utilis* can contain up to 12% of its weight in betulin [11]. Leucocyanidin and polymeric leucoanthocyanidins are also identified components of this plant [12]. The active constituents derived from *Betula utilis* exhibit a wide range of pharmacological activities, including anticancer, anti-inflammatory, anti-HIV, antioxidant, and antibacterial properties (. Betulinic acid, a specific compound found in *Betula utilis*, has been studied for its potential in inhibiting the growth of malignant melanoma and cancers affecting the liver and lungs. This inhibitory effect is attributed to the induction of apoptosis through a direct impact on mitochondria [13].

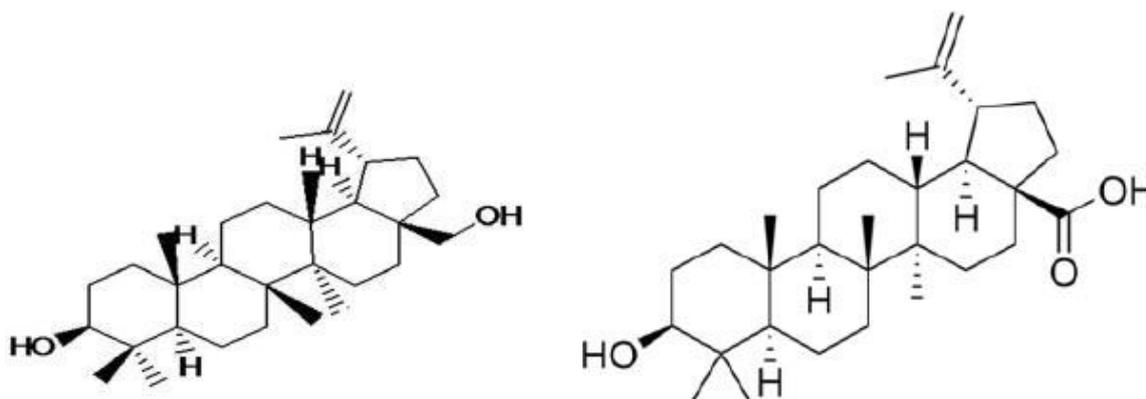


Figure 2. Structure of Betulin and Betulinic acid-Active constituent of *Betula utilis*.

Pharmacological Activities

Antifungal and Antimicrobial

The essential oil extracted from *Betula utilis* exhibits antimicrobial activity. The essential oil from this herb contains various constituents such as geranic acid, seleneol, linalool, sesquiphellendrene, champacol, and 1,8-cineol. These components contribute to the essential oil's bacteriostatic and bactericidal actions against various human pathogens. Moreover, betulinic acid, found in *Betula utilis*, demonstrates broad-spectrum antibacterial activity. It is an easily converted form of betulin and has been shown to be effective against a range of bacteria that pose significant health risks to humans [14].

Anticancer

Betulin, found in *Betula utilis*, can be easily transformed into betulinic acid (3 α -hydroxy-lup-20(29)-en-28-oic acid). Previous research has indicated that betulinic acid reduces the development of liver and lung tumors [15]. Moreover, human melanoma, neuroectodermal, and malignant tumor cells have demonstrated sensitivity to betulinic acid, showcasing its potential impact on the growth of various malignant tumor cells.

Reports have also highlighted the apoptosis-inducing properties of betulinic acid. Apoptosis, particularly in chemosensitive cells, has been associated with various anticancer drugs. Cell mortality induced by chemotherapeutic drugs is often linked to alterations in mitochondrial processes, such as permeability transition. Numerous cancer cell lines, primary tumor tissues, and xenograft animal models have been utilized to explore the antitumor cytotoxicity of betulinic acid. In several studies, betulinic acid has shown significant harm to melanoma cell lines.

Anti-Inflammatory

Methanolic and hydroalcoholic extracts of *Betula utilis* have demonstrated free radical scavenging properties, suggesting the potential to impede the initiation of free radical chain reactions or slow down their progression within an organism. This indicates enhanced anti-inflammatory properties associated with the plant. Studies have shown a reduction in lipoxygenase enzyme activity after inhibition in *Betula utilis*. This suggests that the plant may exert anti-inflammatory effects by neutralizing free radicals. Antioxidants, like those present in *Betula utilis*, can profoundly influence lipoxygenases (LOXs). This influence may involve scavenging lipidoxy or lipidperoxy-radicals generated during enzymatic peroxidation, thereby preventing the formation of lipid hydroperoxide. This, in turn, can contribute to reducing the availability of lipid hydroperoxide for the LOX catalytic cycle [16].

Anti-HIV

There is evidence suggesting that betulinic acid has the ability to inhibit the replication of HIV type 1. Inhibitors targeting the entrance of HIV-1 and HIV-protease have been identified, and they share structural similarities with derivatives of betulinic acid. Various variants of betulinic acid have been discovered to block HIV-1 at a very early stage in the viral life cycle. This finding indicates that these variants might eventually become valuable additions to the standard anti-HIV treatment regimen, which typically includes reverse transcriptase and protease inhibitors [17].

Antioxidant

The bark of *Betula utilis* contains a rich amount of betulinic acid, exhibiting powerful antioxidant action. Beyond its free radical scavenging activity, *B. utilis* also demonstrates free radical reducing activity.

Antiobesity potential of *Betula utilis*

Betulinic acid (BA), a naturally occurring pentacyclic triterpenoid and the main constituent of *Betula utilis*, exhibits a wide variety of pharmacological and biochemical effects. Experimental studies on pentacyclic triterpenoid compounds suggest the inhibition of several enzyme

systems closely related to carbohydrate and lipid absorption/metabolism. BA has been shown to inhibit lipase, α -amylase, protein tyrosine phosphatase 1B, glycogen phosphorylase [18], diacylglycerol acetyltransferase (DGAT), and α -glucosidase. DGAT catalyzes the final reaction of triacylglycerol synthesis, and its inhibition by *Betula utilis* extract can lead to a reduction in triacylglycerol synthesis. In obesity, the accumulation of triacylglycerol in adipocytes, coupled with the consumption of fat-rich foods, can trigger an inflammatory response in the hypothalamus. This disturbance affects anorexigenic and thermogenic signals generated by hormones like leptin and insulin, ultimately leading to an increase in body mass and weight [19]. The inhibitory effect of *Betula utilis* extract on DGAT suggests a potential role in inhibiting adipogenesis. Betulinic acid has also demonstrated pancreatic lipase inhibitory properties, preventing the hydrolysis of ingested fat into absorbable free fatty acids and monoglycerides [20]. This inhibition results in decreased fat absorption and an overall reduction in caloric absorption, contributing to weight loss. Another constituent of *B. utilis*, oleanolic acid, has been reported to improve fatty liver conditions in rats fed a high-cholesterol diet. This effect may be associated with the downregulation of ACAT gene expression, leading to a decrease in intestinal absorption, synthesis, or storage of exogenous and endogenous cholesterol [21-22].

CONCLUSION

Betula utilis, commonly known as Himalayan birch or bhojpatra, holds significant medicinal potential with various pharmacological activities. The plant has been traditionally used for diverse purposes, including its bark being utilized as paper for writing scripts in Sanskrit. With a botanical description provided, *Betula utilis* belongs to the family Betulaceae and exhibits hardiness in the Himalayan region. The chemical constituents of *Betula utilis*, such as betulin, lupeol, betulinic acid, and others, contribute to its therapeutic properties. Betulinic acid, a major constituent, has been found to possess anticancer, anti-inflammatory, anti-HIV, antioxidant, and antibacterial activities. Studies have indicated its potential in inhibiting the growth of malignant tumors and inducing apoptosis in various cancer cells. The pharmacological actions of *Betula utilis*, including its antifungal, antimicrobial, anticancer, anti-inflammatory, anti-HIV, and antioxidant properties, make it a valuable resource for medicinal applications. The plant has been traditionally used in Ayurvedic, Unani, Siddha, and folk medicinal formulations. Moreover, *Betula utilis* shows promise in addressing obesity-related concerns. Compounds like betulinic acid inhibit enzymes involved in carbohydrate and lipid metabolism, such as lipase and DGAT, suggesting a potential role in weight management. Additionally, the plant's ability to reduce lipoxigenase enzyme activity and act as an antioxidant contributes to its anti-

inflammatory effects. In the quest for novel therapeutic agents, *Betula utilis* emerges as a plant of interest, showcasing a rich repository of bioactive compounds with diverse health benefits. Further research and clinical studies are warranted to explore its full therapeutic potential and ensure its safe and effective utilization in modern medicine.

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