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File: ■ Birch (*Betula* spp., Betulaceae)
■ Traditional Use
■ Phytochemistry
■ Pharmacology

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RE: Traditional Uses and Pharmacological Properties of the Genus *Betula*

Rastogi S, Pandey MM, Rawat AKS. Medicinal plants of the genus *Betula* – traditional uses and a phytochemical-pharmacological review. *J Ethnopharmacol*. January 15, 2015;159:62-83.

Birch (*Betula* spp., Betulaceae) bark and bark extracts from this genus of trees and shrubs found in temperate and boreal zones of the Northern Hemisphere are used in the medical traditions of many regions, often for inflammatory conditions such as arthritis. These authors conducted a comprehensive electronic literature search, and review the botany, traditional uses, phytochemistry, pharmacology, and toxicology of birches, discussing therapeutic potential and research needs.

Listed ethnomedicines from every area of birches' distribution include decoctions, teas, baths, pastes, poultices, and powders made from bark, leaves, resin, buds, sap, stems, aerial parts, flowers, roots, cork, and whole plants. Bone-related uses are most common, including microfractures, dislocations, rheumatism, arthritis, and gout. Other reported uses are for urinary and renal ailments, edema, lithiasis, heart problems, skin conditions, hypercholesterolemia, wounds, and burns, among many others. Birch is also used for hair loss. In anthroposophic medicine, its extracts were used in rheumatic diseases. Birches yield sugar, vinegar, and beer. Sweet birch (*B. lenta*) is the main source of oil of wintergreen. Leaf extracts, used as whitening agents in cosmetics, are traditionally used against freckles. Birch bark is a traditional food preservative; in Northern Pakistan it is used to enhance the flavor of ghee during aging. Waterproof, it is also utilized to temporarily cover buildings under construction and to protect harvested crops. In the Himalayan region of India, Himalayan birch (*B. utilis*) is used in religious ceremonies.

While naming many species and their habitats, distribution, and uses, the authors note that the taxonomy of European birches is disputed due to morphological variability and hybridization. Inability to distinguish among closely related species has prompted biometric and chemotaxonomic studies, as well as studies of phylogenetic relationships. Chemotaxonomic studies have focused mainly on phenolics (flavonoids and terpenoids) in birch bark, leaves, buds, and stems. This review lists 137 triterpenoids (from the ocotillol; dammarane type I, II, III, and IV; oleanane; and lupane groups); diarylheptanoids (cyclic and acyclic); phenylbutanoids; phenolics; flavonoids, flavones, and flavanones; catechins and lignans; steroids; and miscellaneous compounds from birches, with the species from which they were isolated. More importantly, the chemical composition of extracts can vary

significantly between plant parts and processing methods. Three triterpenoids – betulin, betulinic acid, and lupeol, belonging to the lupane group and found in all birches – are especially noteworthy, as is papyriferic acid, secreted by glands on twigs during only the juvenile ontogenetic phase of resin-producing tree birches. Several reviews of betulin, lupeol, and betulinic acid have been published. Accompanying figures illustrate the chemical composition and basic structure of these compounds.

Pharmacological studies report anticancer, anti-inflammatory, antiarthritic, antioxidant, antimicrobial, antiviral, dermatological, immunomodulatory, hepatoprotective, antidiabetic, gastroprotective, and other effects for birch species, parts, extracts, and compounds. For example, anticancer effects from several birch species and/or extracts have been reported against 12 different human and murine cancer cell lines. Against A431 skin epidermoid carcinoma, the 70-80% inhibition of proliferation seen in vitro for a silver birch (*B. pendula*) bark extract and its two main constituents, betulin and betulinic acid, may be of practical significance; a pilot study of a birch bark ointment in actinic keratosis also reported efficacy with no adverse effects after two months of use. In an MTT [3-(4,5-dimethyl-2-thiazolyl)-2,5-diphenyl-2H-tetrazolium bromide] assay using four cancer cell lines comparing several betulin-enriched extracts, all of the prepared bark extracts exerted a pronounced antiproliferative effect against human cancer cell lines. The substantial differences in betulin and betulinic acid content were not reflected in antiproliferative activity. While this may be attributed to other active natural birch compounds, including flavonoids, the authors comment on the micromolar and even nanomolar quantities needed for birch's effects to occur, comparable to some synthetic drugs. An evaluation of birch triterpenes against human cancer and multidrug-resistant (MDR) cell lines, while reporting no significant differences in cytotoxicities of the tested compounds against sensitive and resistant cell lines, found that cytotoxicity for several compounds in resistant lines was enhanced in the presence of non-toxic amounts of colchicine or doxorubicin, raising the possibility of MDR reversal. Papyriferic acid, which in nature protects immature birches from browsing by mammals, has also been studied in MDR cancer cells; several of its derivatives exhibit potent MDR-reversing ability.

While most studies of birch and birch extracts have been in vitro or in vivo, a few human trials besides the skin cancer pilot study mentioned are referenced. It was reported that white birch (*B. pubescens* syn. *B. alba*) leaves and buds have been used to treat uterine cancer; no details are provided. Also, a study of a white birch extract in chronic hepatitis reported subjective symptom reductions as well as objective outcomes, and monitored safety and compliance.

Pharmacological studies support traditional uses of birch bark and birch extracts in bone-related problems such as degenerative joint disease and demonstrate a variety of effects that contribute to bone and joint health. Traditional use in wound healing, hypercholesterolemia, and bile disorders is also supported. While no ethnopharmacological link seems to exist between traditional uses and the current interest in birch extracts as novel anticancer compounds, many traditional uses imply modification of the cell cycle, and the pharmacological evidence for these compounds is strong. Controlled, clinical trials are needed to determine if there is a basis for other traditional uses and claims.

—Mariann Garner-Wizard

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