REVIEW ARTICLE

Taxonomy, Ontogenesis, Biochemical Composition, and Biological Activity of *Hypericum scabrum* L. (*Hypericaceae* Juss.): An Overview

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ABSTRACT

This review aims to provide updated and generalized data on ethnobotany, ontogeny, phytochemistry, and biological activity of *Hypericum scabrum* L. This plant has long been used as a medicinal plant in traditional medicine in Turkey and Iran and the republics of the Caucasus and Central Asian region, but not presented in official medicine. Essential oils, terpenoids, flavonoids, anthraquinones (hypericin and pseudohypericin), hyperforin, and other compounds were determined during the phytochemical analysis of this species. An overview of the content and distribution of specific biomarker compounds (i.e., those suspected of being relevant to the pharmaceutical industry) and studies of extracts and individual isolated compounds is presented. Medicinal plant raw materials possess high bioavailability, the absence of toxicity, a wide range of biological activity, and high therapeutic potential. Further study of *H. scabrum* L. is required to include it in the list of medicinal plant species of official medicine and determine its prospects as a source of modern herbal drugs.

***Keywords*:** Biochemical composition, Biological activity, *Hypericum scabrum*, Hypericin, Hyperforin, Ontogenesis, Taxonomy.

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INTRODUCTION

Hypericum scabrum L. is one of the perennial and herbal medicinal plants belonging to *the Hypericaceae family;* floral on aerial parts of this plant have been widely used to prepare traditional medicines. This review tried to collect and analyze all contemporary and generalized data for ethnobotany, ontogeny, phytochemistry, and biological activity issues of *H. scabrum* L.

MATERIALS AND METHODS

Analysis of domestic and foreign literary sources of different years has been carried out. Electronic scientific search engines (Pubmed, Springer, Wiley Online Library, Science Direct, Biodiversitylibrary), electronic databases (Pubchem, Human Metabolome Database), and other Internet resources were used to search for relevant literature and information.

RESULTS AND DISCUSSION

Phylogeny, Taxonomy, Botanical Description and Distribution

For a long time, taxonomists debated whether the genus Hypericum and its closest relatives should be considered a separate family (*Hypericaceae*) or as a subfamily of *Hypericoideae* within *Guttiferae* (*Clusiaceae*).[1-7] A new opportunity to identify family relationships between living organisms based on the study of the structure of polymer macromolecules (DNA, RNA, proteins) appeared in the last decades of the 20th century. Family ties within the *Guttiferae* s. l. were established in 1993 by molecular phylogenetic methods based on the analysis of nucleotide sequences of the *rbcL* gene; the complex was first identified as a monophyletic group.[8] Further studies by the Angiosperm Phylogeny Group (APG), based on genetic traits, allowed the inclusion of *Guttiferae* s. l. in the *Clusioid* clade, with the composition of the *Hypericaceae*, *Caryophyllaceae*, *Clusiaceae*, and *Bonnetiaceae* families, and also made it possible to detect genetic links with *Podostemaceae* (the closest to *Hypericaceae*). The clade was assigned to the order *Malpighiales*; this order includes over 16,000 species and is one of the most significant orders of angiosperms.[9-12] In the traditional classification of flowering plants of the 20th century,[1,2] the *Malpighiales* order was not distinguished.

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In recent Angiosperm Phylogeny Group (APG) research, the *Clusioid* clade is included in the *Rosids* group (*Malvids* clade).[13] Numerous molecular phylogenetic studies have confirmed that *Hypericaceae* is a separate family, independent and monophyletic, distinct from other members of the *Guttiferae* s. l.[12,14-17] Cladistic analysis of the genus showed that *Hypericum* sp. monophyletic (including the monotypic genus *Santomasia*). An essential group-containing Mediterranean species (assumed to be of Mediterranean origin) and three large clades containing most of the genus diversity were identified. In addition, it was found that the shrub life form was the ancestral state from which the arboraceous and herbaceous groups evolved; it was also found that apomixis occurred at least three times independently within the genus.[18]

Family *Hypericaceae* Juss. (HYP)[19] includes 540–560 plant species distributed in tropical, subtropical, and temperate regions of both hemispheres, except very cold or very dry areas.[6,7,20] Nine genera were taxonomically classified as *Hypericaceae*: *Cratoxylum* Blume, *Eliea* Cambess., *Harungana* Lam., *Hypericum* L., *Lianthus* N. Robson, *Santomasia* N. Robson, *Thornea* Breedlove & E.M. McClintock, *Triadenum* Raf., and *Vismia* Vand.[6,7]

Genus *Hypericum* L. - St. John's wort**.** Etymology: *Hyper-* (Greek) - above; *eikon* (Greek) – picture, image; *υπερεικον* is the name given by Dioscorides ("*De Materia Medica*"), due to the use of the species of St. John's wort over shrines and religious images to ward off evil spirits.[21,22] The genus includes 490–500 species of perennial or annual herbaceous plants, semi-shrubs, evergreen or deciduous shrubs, and trees (up to 12 m high); plants are distributed mainly in the temperate regions of the Northern Hemisphere, as well as in mountainous and alpine subtropical and tropical regions, at an altitude of up to 3000–5000 m above sea level. Representatives of the genus are absent in tropical lowlands, hot and cold deserts, one European species (*H. elodes*) is a typical hydrophyte. About 80% of the diversity of species of the family is within the St. John's wort genus.[22-25] The Mediterranean region is the center of species diversity, especially rich in representatives of the genus Turkey (96 species, 47 of which are endemic).[26,27] Other regions are less rich in representatives of the St. John's wort genus; nevertheless, they include significant numbers of taxa: 64 species in China,[28] more than 60 species in the flora of Europe,[29] 58 species in the USA and Mexico,[22] more than 70 species in Central and South America (including 23 species in Brazil),[30] 32 species in Transcaucasia,[31] 22 species in Russia.[32,33] Australia is the poorest in the genus; in the flora of Australia, only 2 native species have been recorded.[34] The most famous thoroughly studied and widespread species introduced or adventive in almost all world regions (including Australia) is *Hypericum perforatum* L.[24]

Detailed intrageneric classification and morphological description of all known taxa *Hypericum* sp. are presented by the English botanist Norman Robson (born 1928) in a series of monographic works of world importance published in 1977 to 2012.[4,5,25,35-43] The whole variety of the genus is distributed over 36 sections and many subsections.[4,24,44] *H. scabrum* L. is included in sect. 17. *Hirtella* Stef. subsect. *Platyadenum* N. Robson; this section includes 30 species distributed mainly in the Mediterranean region, including North Africa (Morocco) and West and Central Asia. These are perennial herbaceous plants up to 0.8 m height, glabrous, pubescent, and with simple or branched glandular emergences, often glaucous, with erect or decumbent at the base stems (with 2 lined filiform ridges) and rarely rooting tap root; usually with creeping to ascending sterile basal shoots with axillary branches (often numerous and densely located); bracts and bracteoles have a characteristic oblong-lanceolate or linear shape. Accumulations of specialized secretory cells (in the form of colored dots) are located on the petals, are common on sepals and bracts, sometimes located on stems and leaves, but absent on anther ligaments and fruits.[43]

H. scabrum L. (syn. *Drosanthe scabra* (L.) Spach, *H. asperum* Ledeb, *H. cymosum* Hochst, *H. galioides* Freyn & Sint.) is a perennial herb with a height of (4-) 10-45 (-60) cm, with a woody taproot with a length of 16–29 cm and a diameter of 0.4–1 cm and numerous shoots that are differently oriented in space (plagiotropic, orthotropic and anisotropic). Reproductive shoots are erect or ascending, branched from the base, with sterile short ascending axillary branches; vegetative shoots are creeping with ascending axillary branches, and ascending, usually highly branched (enrichment shoots).

Stems of orthotropic shoots are rigid, glabrous, red or reddish-brown, often with a glaucescent bloom, rounded in cross-section, with 2 lined filiform ridges (very rarely from 3 to 5),[45], scabrous, with randomly located (especially numerous in the basal parts) warty simple emergences with a red glandular apex, less often smooth or almost without epidermal outgrowths. The leaves are simple, opposite, sessile or almost sessile (petiole up to 0.3 mm long), without stipules, free, slightly leathery or herbaceous, glabrous, green, sometimes glaucescent, with numerous small translucent laminar and marginal glands; the venation is camptodromous, single-veined, with a well-visible central and (1) 2 thin, weakly noticeable lateral veins extending from the base of the central vein. The leaf blades are dimorphic. On the main stems of reproductive shoots and enrichment shoots, the leaves have an oblong, oblong-elliptical, lanceolate, less often linear shape, 0.7-2 (-2.7) cm long and 1.5–7 mm wide, with wedge-shaped bases, rounded or pungent, sometimes hooked apex, and whole, often slightly curled edges. The leaves of axillary and vegetative shoots are smaller and sharper, 0.3–1 cm long and about 1 mm wide, linear, with strongly curled edges (Figure 1).

Inflorescences are terminal, cymoid, (1-) 5-flowered, monochasial, or dichasial-monochasial, with 2-13-flowered lateral monochasia, acrotonally localized and form dense bracteous corymbose or corymbose-capitate synflorescence 0.5-8 (-11) cm long and up to 6 (-9) cm wide. Bracts and bracteoles sessile, herbaceous, green, deciduous together with leaves, oblong-lanceolate or linear, 1–3 mm long and up to 0.7 mm wide, with pungent apices and membranous, irregularly glandular-serrate margins, less often almost smooth-margin; marginal glands black, usually located closer to the apex of

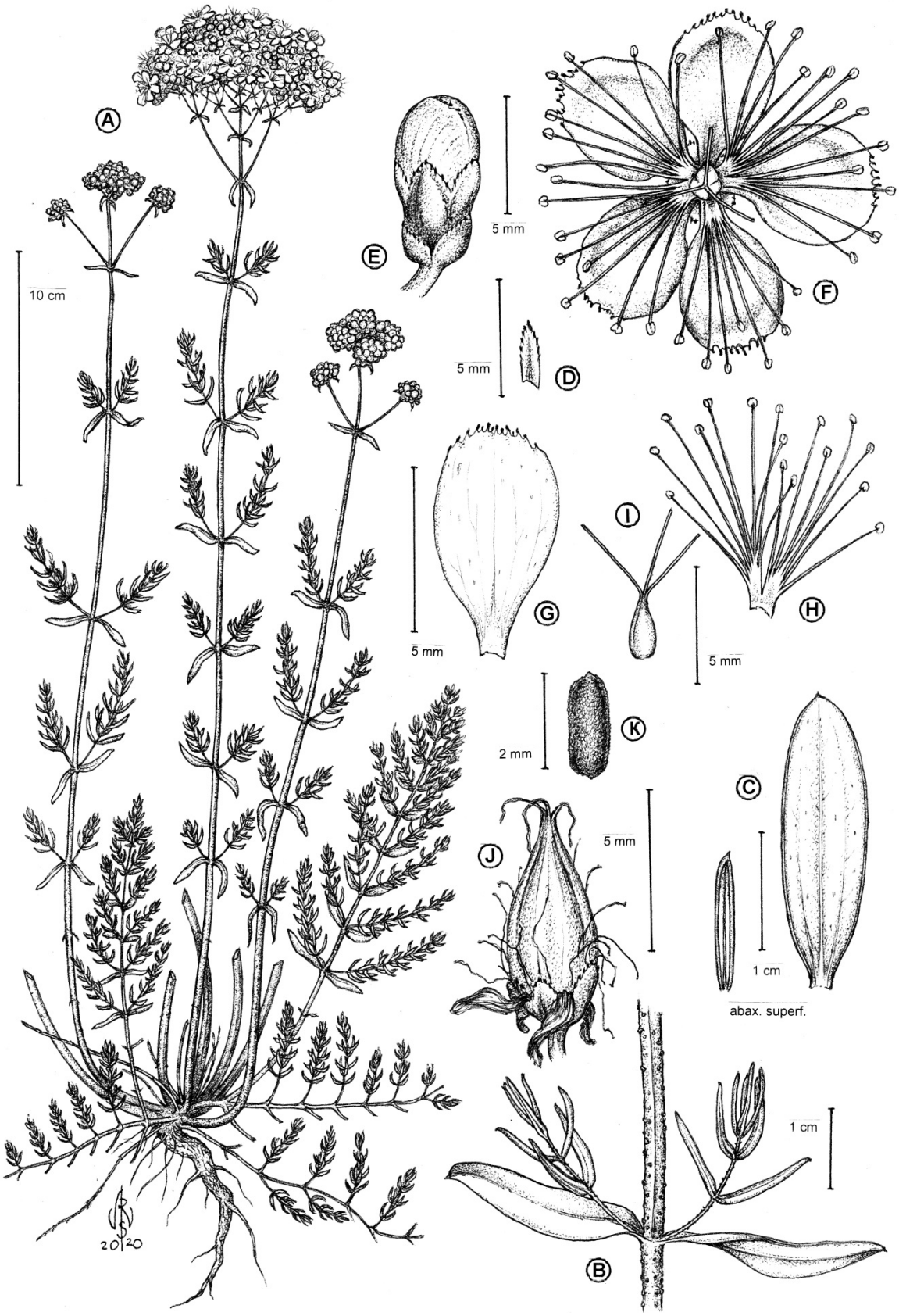

Figure 1: *Hypericum scabrum* L.: A. External appearance. B. Leaf and portion of stem. C. Leaves. D. Bracteole. E. Bud. F. Flower G. Petal. H. Stamens (double fascicles). I. Ovary. J. Fruit. K. Seed.

the lamina. Flowers are bisexual, homostylous, actinomorphic, cyclic, with a double perianth, stellate (with horizontally bent petals), 0.5–1.6 cm in diameter, on slender naked pedicels 1–3 mm long; buds are erect, spherical or spherocylindrical, with rounded apices. Calyx green, glabrous, campanulate, of 5 equal, basally connate by 1/3–2/3 of the length of the sepals; the calyx is persistent in fruit. Sepals are oblong, 1–2.5 mm long and 0.7–1.2 mm wide, with rounded or slightly pointed apices, 3-veined, with laminar translucent glands (in the form of two lines) and membranous, irregularly glandular-serrate or glandular-ciliate margins, less often ciliate without glands or almost smooth-margins; marginal glands are black, elliptical, rounded or irregular. Petals are equal, slightly asymmetric, glabrous, bright yellow, oblanceolate, oblong-obovate or obovate, (3–) 5–8 mm long, and (1-) 2–3 (–5) mm wide, with unguiculate bases (up to 2 mm long) and smooth margins, veiny, with laminar translucent glands (in the form of dots or short dashed lines). The apices are rounded, irregularly glandular-long-ciliate, less often almost smooth-margin, with marginal black glands of elliptical, round or irregular shape (very rarely the glands are not developed). Stamens 25–45, on slender naked yellow filaments (4–8 mm long), fused basally in 3 bundles; 5 fascicles opposite the petals are differently connected (2 + 2 + 1): four double fascicles are located opposite the sepals.

Anthers small, bright yellow, round-elliptical, 4-locular, parallel thecae, introrse, opened up by longitudinal slits; connective with the terminal orange-yellow translucent gland. Pollen grains are monad, with a medium size (length of the polar axis 26.5–28.6 μm; length of the equatorial axis 20.5 –22.5 μm), triangular in the polar outline, tetrahedral, irregular, heteropolar in the equatorial outline, with 6-zonal colporate aperture and reticulate microporous exine sculpture.[46,47] The gynoecium is coenocarpous, of 3 carpels, with free slender stylodia diverging from the base, 2-5 mm long, with apical punctiform stigmas. Ovary superior, glabrous, greenish-yellow, narrowly ovate, 1-3 mm long and up to 1.5 mm in diameter, narrowed towards the apex, 3-locular, with angular placentation and numerous ovules on each placenta.

The fruit is a superior fragmocarpous capsule, ovoid, (3–) 4–8 mm long and 2.5-5 mm in diameter, pointed, with remnants of stylodia at the apex, leathery, glabrous, slightly furrowed, reddish-brown in color, septicidal from apex; valves sometimes with prominent lateral resiniferous canals. The fruit base is enclosed in a persistent calyx with fragmentary remnants of dried petals and stamens. Seeds are usually numerous, cylindrical, 1.5–2 mm long, obtuse, dark brown, papillose white villous spermoderm, without endosperm, slender straight embryo, and equal cotyledons. Papillae are erect, rounded, with a smooth surface; in the cells of the integumentary layer of the spermoderm, a significant amount of angular crystals of calcium oxalate was noted[48] $2n$ = 24, 28,?48.[28,43,49-53,58]

The area covers northwest China (Xinjiang Uygur Autonomous Region, Altay Prefecture), Central Asia (Kazakhstan, Kyrgyzstan, Tajikistan, Turkmenistan, Uzbekistan), Afghanistan, Pakistan, Transcaucasia, and Western Asia (Israel, Lebanon, Syria, Turkey, Iran, Iraq).[27,28,31,43,50,52-55] In "Flora of the USSR"[51] it is erroneously indicated for Russia: "Western Siberia: Altai"; does not appear in later floristic reports.[32,56,57] Plants grow on dry rocky and gravelly open slopes, juniper forests, wormwood, shrub thickets, woodlands, calcareous taluses, rocky outcrops, from foothills to the upper belt of mountains, at an altitude of 3300 m above sea level.[59,60]

Ontogenesis and Phenology

The habitual characteristics of the stages of the large life cycle of *Hypericum scabrum* L. correspond to the periodization of ontogenesis of perennial herbaceous plants developed by Rabotnov T.A.,[61] supplemented by Uranov A.A.[62] and Vorontsova L.I.[63] The life cycle is subdivided into three periods: pre-generative, generative, and post-generative (senile).

*Pre-generative period. S*eedlings with tap root, hypocotylary, orthotropic, with cotyledonous leaves, 3-6 internodes, and a series of first true leaves. Juvenile individuals are characterized by the falling of cotyledon leaves, lodging of the shoot in the hypocotyl part, and further development in a plagiotropic direction; lateral vegetative shoots with shortened internodes develop from the axillary buds of the distal shoot nodes. In immature individuals of the second year of life, the first orthotropic vegetative shoots develop from the renewal buds, which are located in the axils of the fallen cotyledon leaves, and the development of the plagiotropic shoot continues due to the lodging of the first-order shoots. Virginile individuals form 3-6 vegetative orthotropic shoots 10 to 12 cm high and develop a powerful taproot system with a branched main root; adult vegetative plants produce 10-15 orthotropic shoots 20–25 cm high and 2-5 (-10) plagiotropic shoots. The pre-generative period lasts 2 to 5 years and is transitional to the generative one; the duration of the period may increase with increasing altitude. The development of orthotropic vegetative shoots is confined to the spring period, plagiotropic ones - to the autumn-winter period after the orthotropic shoots die off.

Generative period. Flowering begins in the sixth or ninth year of life; in the first year, flowering is most intense, characterized by a large number (from 6 to 13) orthotropic generative and vegetative shoots. In the second year of flowering, the flowering intensity decreases, and the assimilating area decreases (old generative individuals).

Postgenerative period. Reproductive orthotropic shoots are not formed; vegetative shoots are few in number and depressed; plagiotropic shoots practically do not develop (the habit of juvenile plants is manifested). There is intense peeling of the cork and the dying-off of lateral roots at the roots; destructive processes continue for 1 to 2 years. The plant's life cycle from seed germination to dying off is 8 to 13 years, with a short (1–2 years) generative period; there is a monocarpic tendency. The life form of the plant is a dwarf shrub of a group of summer-winter-green plants with two generations of leaves per year: leaves of the autumn generation are formed in November and stay green throughout the winter (they die off in June-July); leaves of the spring-summer generation develop

in March.[49,64] Flowering: May-July (Central Asia, Pakistan, China); [28,50,52,53,60] May-August (Syria, Palestine).[54] Fruiting: August-September (China);[28] June-August (Uzbekistan).[52]

Anatomy

Orthotropic shoots are round in cross-section with triangular projections of longitudinal filiform ridges and emergence. Epidermal tissue consists of rectangular or nearly square cells with thickened outer walls and cuticular covering. The peripheral part of the primary cortex is presented by 2–3 (less often one) rows of lamellar collenchyma; the number of rows of collenchyma increases to 5–8 in the projections of the ridges and emergence. 2-3 rows of chlorenchyma are located below; in deeper layers, it turns into a 2-3-row collenchymatous parenchyma with thickened tangential cell walls. The basal part of the primary cortex is presented by a single-row layer of rectangular cells of the endoderm. Conductive tissues have an annular arrangement with single-row medullary rays. The cambial zone is indistinct. Secretory canals, lined by a row of flattened cells, are located in the phloem zone.

The leaves of orthotropic shoots with a normally developed leaf blade have a dorsoventral structure. The epidermis has a well-developed cuticle of almost rectangular cells. Palisade chlorenchyma (2-3 layers) are located on the adaxial surface under the epidermal tissue. Spongy chlorenchyma (1-2 layers) with loosely located cells adjacent to the epidermal tissue of the abaxial leaf surface is located below the palisade chlorenchyma. Xeromorphic, linear leaves are sometimes isolateral (with palisade chlorenchyma located on both sides of the leaf) or equifacial type (with a homogeneous, almost undifferentiated mesophyll). The mesophyll contains large secretory canals with a large lumen lined by a row of flattened cells. Usually, the canal diameter coincides with the thickness of leaf mesophyll; the canal adjoins the upper and lower epidermis cells from the inside. The main vein is presented by collateral vascular bundles surrounded by parenchymal cells and a 1-2-layer abaxial collenchyma covering; narrow secretory canals are located in the phloem zone. The epidermis of the adaxial and abaxial leaf surfaces is presented by oblong, polygonal cells with characteristic lenticular thickening of the walls; cells located above schizogenous receptacles have uniformly thickened walls. The stomata are developed on both leaf surfaces (amphistomatic lamina) or on the lower surface (hypostomatic lamina of a xeromorphic leaf). The stomatal apparatus is anisocytic; guard cells are surrounded by three unequal subsidiary cells.[45,49,64-66]

Examination of leaves on specimens from Iran revealed hair-like structures of a triangular, finger shape, and star-shaped papilla in their epidermis;[67] no trichomes were found on samples from Turkey and Tajikistan.[45,49] In addition, the structure of the epicuticular wax layer of the epidermis has been studied: epidermal cells carry only one type of wax crystals in the form of randomly arranged rodlets (crystalloid type).[67] Genus *Hypericum sp.* characterized by the presence of various types of secretory structures: the so-called "pale" or "translucent" glands (cavities) and "dark" or "black" glands (nodules), as well as resinous channels of schizogenic origin. "Dark" glands are the essential structures and are used as a distinguishing feature for classifying the genus and intrageneric subdivisions.[4,68] "Pale" glands have the appearance of transparent, yellowish, or orange-yellow dots, scattered on the stem, leaves, sepals, and petals, found in all representatives of the genus. The glands are located at different depths in the mesophyll or subepidermal. The glands are schizogenous cavities lined with flattened epithelial cells and containing essential oil and phloroglucinol derivatives.[69-73]

Large secretory canals with a large lumen (type B) are located within the leaf mesophyll and sometimes merge with the "pale" glands; smaller canals with a smaller lumen (type A) are localized in the phloem and are especially noticeable in the vascular bundles in the first-order and second-order veins. The third type of canals (type C) was found in the tissues of the ovary and stylodia. Histochemical studies have shown that phloem reservoirs do not contain essential oils but that alkaloids, lipids, and resins accumulate in them.[70,73] "Dark" glands are typical only of *Hypericaceae.* They have reddish or almost black dots, usually localized at the edge of leaves, petals, and sepals (not found in all taxa). The origin of the glands is not schizogenic or lysogenic; they are clusters of excretory cells of irregular shape, enclosed in a 2–3-layer membrane of flattened cells and containing granular secretion, in which anthraquinone derivatives (hypericin, pseudohypericin) accumulated.[5,71,74-76]

Ontogenetic, Morphogenetic, and Diurnal Variability of Phenolic Compounds

Secretory structures ("pale" and "dark" glands, resinous canals) are sites of synthesis and/or accumulation of biologically active substances, the localization of which is different depending on the plant organ.[70] The organ dependence of the content of biologically active substances plays an important role in understanding the accumulation of phenolic compounds during the phenological and diurnal cycles of plant development. The leaves of *H. scabrum* L. have a higher content of phenols in comparison with other tissues, and the content of phenolic compounds in the whole plant reaches its maximum level in the budding phase at noon (0.24% DW), then decreases; the highest value (0.32% DW) was obtained for flower buds harvested at noon (Turkey).[77]

Anthraquinone derivatives (hypericin, pseudohypericin) are localized in leaves and reproductive organs and are not found in stem tissues. The highest concentration of these substances is observed in the reproductive organs. In the budding phase, the maximum values of the content of hypericin and pseudohypericin in flowers (0.18 mg/g DW and 0.19 mg/g DW) and leaves (0.095 mg/g DW and 0.12 mg/g DW) (Turkey) are reached. *H. scabrum* L. produces low to moderate amounts of both forms of hypericin compared to *H. perforatum* L., the well-known commercial source of anthraquinones.[78] "Dark" glands reach full development and maturity earlier than the organ on which they are located; clusters of excretory cells are probably no longer metabolically active, but they only function

as reservoirs. This may explain why the highest percentage of anthraquinone derivatives is found in the budding phase.[74,79]

Ethnobotany

H. scabrum L. has long been used in traditional folk medicine. In Turkey, infusions and decoctions from the aerial part are widely used as an antispasmodic, sedative, antiseptic, antifungal, anthelmintic, antiulcer, and anti-inflammatory agent as for the treatment of hemorrhoids, constipation, gastric and duodenal ulcers. In the form of an ointment, infusions and decoctions are used for psoriasis, ringworm, eczema, and as a wound-healing agent.[80-86] In Tajikistan, the herb is used to treat diseases of the liver, heart, gastrointestinal tract, bladder, cough; in the form of a poultice, the herb is used to treat ulcers, abscesses, abscesses, boils, and mastitis; infusion of flowers is recommended for jaundice.[87] In Uzbekistan, the plant is one of the most popular medicinal herbs and is used to treat heart, liver, gallbladder, gastrointestinal tract, rheumatism, and cystitis.[88,89]

In Kazakhstan, infusions and decoctions from the aboveground part are used for joint diseases, rheumatism, acute colds, tuberculosis, fever, inflammatory processes of female genital organs, urinary incontinence in children, for the treatment of neoplasms, and as an anthelmintic; externally, the plant is used in the form of ointments and compresses, for burns, bedsores, non-healing wounds, childhood diathesis, vitiligo, ulcers and fistulas.[90,91] In traditional Iranian medicine, the herb of *H. scarbum* L. is used as an anticonvulsant, and flowers are used for stomach ulcers, migraines, urinary incontinence, and bleeding.[92,93] In close cultures of Western and South Asian countries (Turkey, Iran, Azerbaijan), flowers and herb in the form of infusions and decoctions are used as an anesthetic and sedative, as well as for constipation, hemorrhoids, jaundice, menstrual irregularities, kidney and stomach diseases.[94] In addition, in Central Asia, the yellow dye is obtained from flowers; the acidic extract from the flowers produces red and pink dyes.[50]

Biochemical Composition

Alicyclic compounds: (2*R*,3*R*,4*S*,6*R*)-3-methyl-4,6-di(3-methyl-2-butenyl)-2-(2-methyl-1-oxopropyl)-3-(4-methyl-3-pentenyl)-cyclohexanone – in aerial part;[95] 3-cyclohexene-1-ol – in callus (hypocotyl explants).[96]

Iridoids: 4aα,7α,7aβ-nepetalactone, 4aα,7β,7aα-nepetalactone - in aerial part.[97]

Monoterpenoids: borneol, bornylacetate, camphene, *p*-cymene, limonene, β-myrcen, (*Z*)-β-ocimene, (*E*)-*β*-ocimene, α-phellandrene, *β*-phellandrene, α-pinene, *β*-pinene, pulegone, α-terpineol, α-thujene - in aerial part and callus (hypocotyl explants);[96-108] α-campholenal, γ-campholenal, α-campholenic acid, camphor, δ-3-carene, *cis*-carveol, *trans*-carveol, carvone, 1,8-cineol, *o*-cymene, *p*-cymen-8-ol, eukarvone, α-fenchene, fenchol, (*E*)-geranylacetone, isopinocamphone, linalool, *cis*-linalool oxide (furanoid), *trans-m*-mentha-2,8-diene, *p*-mentha-1,5-dien-8-ol, *p*-mentha-1,8-dien-4-ol (limonen-4-ol), *cis-p*-mentha-1(7),8-dien-2-ol, o-mentha-1(7),5,8-triene, *cis-p*-menth-2-en-1-ol, *trans-p*-menth-2-en-1-ol, menthone, myrtenal, myrtenol, myrcene, neoalloocimene, α-pinene oxide, *trans*-pinocamphone, *trans*-pinocarveol, pinocarvone, piperitenone, piperitenone, piperitone, sabinene, *trans*-soberol, α-terpinene, γ-terpinene, terpinen-4-ol, terpinolene, thuja-2,4-diene, thuja-2,4(10)-diene, β-thujone, *trans*-verbenol, verbenone, *cis*-verbenylacetate - in aerial part (Table 1).[97-101,104-108]

Sesquiterpenoids: α-amorphene, aromadendrene, bicyclogermacrene, *γ*-cadinene, δ-cadinene, α-cadinol,

Table 1: Main components of essential oil (%) *H. scabrum* L.

State	*Plant part*	*Components*	*Sources*
Uzbekistan	aer. part	α-pinene (11,2%), spatulenol (7,2%), *p*-cymene (6,1%), acetophenone (4,8%), carvacrol (4,7%)	[98]
Tajikistan	aer. part	α-pinene (44,8%), spatulenol (7,1%), verbenone (6,0%), *trans*-verbenol (3,9%), γ-muurolene (3,5%)	[104]
Turkey	aer. part	α-pinene (71,6%), β-caryophyllene (4,8%), myrcene (3,8%), cadalene (3,4%), β-pinene (2,9%)	[99]
Turkey	aer. part	α-pinene (74-83,3%), β-pinene (4,1-4,8%), myrcene (3.4%)	[107,130]
Turkey	aer. part	α-pinene (51,3 %), β-pinene (7,7 %), spatulenol (3,4 %)	[105]
Turkey	aer. part	α-pinene (9,26%), terpinen-4-ol (5,12%), camphor (5,94%), δ-cadinene (4,52%), pulegone (4,45%), γ-muurolene (4,12%), pinocarvone (3,97%), β-caryophyllene (3,42%)	[97]
Turkey	aer. part	α-pinene (42,3%)	[131]
Turkey	aer. part	α-pinene (45,3%), *n*-nonane (5,6%), thymol (5,3%)	[129]
Iran	aer. part	α-pinene (40,9 %), spatulenol (7,9 %), β-pinene (5,2 %), *α*-cadinol (4,7 %), limonene (4,3 %), *epi*-α-muurolol (3,2 %)	[100]
Iran	aer. part	α-pinene (49,96-59,3%), *β*-pinene (4,1-9,7%), limonene (2,1-6,66%), carvacrol (5,84%)	[101,128]
Iran	flow., fruits	α-pinene (70,21%), *p*-mentha-1,5-dien-8-ol (2,89%)	[132]

β-caryophyllene, caryophyllene oxide, *α*-copaene, *β*-cubebene, *β*-elemene, germacrene D, α-humulene, isospathulenol, β-selinene - in aerial part and callus (hypocotyl explants);[96-108] bicycloelemene, β-eudesmol - in callus (hypocotyl explants);[96] alloaromadendrene, *trans*-*α*-bergamotol, *β*-bisabolene, *α*-bisabolol, *β*-burbonene, cadalene, *α*-cadinene, δ-cadinol, *epi*-α-cadinol, *α*-calacorene, *β*-calacorene, γ-calacorene, *cis*-calamenene, *trans*-calamenene, caryophylladienol-I, 9-*epi*-(*E*)-caryophyllene, caryophyllenol-I, caryophyllenol-II, *α*-cubebene, cubenol, 1-*epi*-cubenol, α-farnesene, (*E*,*E*)-α-farnesene, (*Z*)-β-farnesene, γ-farnesene, (*Z*,*Z*)-farnesylacetone, globulol, α-guaiene, *α*-gurjunene, β-gurjunene, γ-gurjunene, 4,1-herbertenolide, humulene epoxide-II, isocaryophyllene oxide, 4-Isopropyl-6-methyl-1,2,3,4-tetrahydronaphthalen-1-one, ledol, *α*-longipinene, *cis*-muurola-4(14),5-diene, α-muurolene, *γ*-muurolene, *T*-muurolol, *epi*-α-muurolol, 1,5-*epoxy*-salvial(4)14-ene, salvial-4(14)-en-1-one, 4,11-selinadiene, α-selinene, *β*-selinene, δ-selinene, γ-selinene, spathulenol, *cis*-tetrahydrojasmine, valencene, viridiflorene, viridiflorol, ylangene, *oxo*-α-ylangene - in aerial part.[97-109]

Diterpenoids: phytol – in aerial part, seeds and callus (hypocotyl explants);[96,101-103,105,106] *ent*-beyer-15-en-18-ol, *trans*-geranylgeraniol, *geranyllinalool* – in aerial part.[109]

Triterpenoids: squalene – in stems and seeds.[102,103]

Steroids: γ-sitosterol – in stems;[102] 22,23-dihydrostigmasterol – in leaves, stems, and seeds[102,103] ergosterol, β-sitosterol, stigmasterol – in flowers[110]

Derivatives of Benzene: acetophenone, benzylbenzoate, (*Z*)-3-hexenylbenzoate, *p*-methylacetophenone – in aerial part.[97,98,100,104]

Derivatives of Phenol (phloroglucinol and derivatives): 17*R*,18-dihydroxyfurohyperforin, (1S,32R,5S,6R,7R)-6-((R)-3,4-di-hydroxy-4-methylpentyl)-2-(2-hydroxypropan-2-yl)-7-isobutyryl-6-methyl-5,9-bis(3-methylbut-2-en-1-yl)-4,5,6,7-tetrahydro-2H-32,7-methanocycloocta[b]furan-8,10(3H)-dione, (4R,5R,7R)-4-((R)-3,4-dihydroxy-4-methylpentyl)-2,2,4-trimethyl-5,7-bis(3-methyl-but-2-en-1-yl)-7-(5-methylhex-4-enoyl)-4,5,6,7-tetrahydrobenzofuran-3(2H)-one, furoadhyperforin isomer 2A, furoadhyperforin isomer 2B, furohyperforin isomer 2, hyperibones A – L, hyperibrins A - G, *Hypericum*oxides A - N, hyperscabrins A - M, hyperforin, phloroglucinol, scrobiculatone B - in aerial part.[88,89,95,108,111-118,168]

Phenolcarboxylic Acids and Derivatives: benzoic, chlorogenic – in aerial part;[109,119,120] neochlorogenic – in leaves and flowers;[120] caffeic, hydroxycinnamic, 2,4-dihydroxybenzoic, ferulic, rosmarinic, vanillic – in flowers;[110,120] bis(2-ethylhexyl)phthalate – in leaves, stems, flowers, and seeds;[102,103] dibutylphthalate – in seeds.[102,103]

Phenylpropanoids: thymol – in aerial part, seeds, and callus (hypocotyl explants);[96-98,101-103] carvacrol - in aerial part and callus (hypocotyl explants);[88,96-98,101-103,105,106,108] cuminol, elemicine, estragole (1-methoxy-4-(2-propenyl)benzene), isocarvacrol, isopropenyltoluene, Isopropyl phenyl ketone, isothymol, myristicin - in aerial part.[88,98,105,106,108,109]

Polycyclic aromatic hydrocarbon: naphthalene - in aerial part and callus (hypocotyl explants).[96,109]

Flavonoids: morin – in flowers;[110] avicularin, apigenin 7-*O*-glucoside, hyperin, hyperoside, isoquercitrin, kaempferol, luteolin, myricetin, myricetin 3-*O*-a-L-rhamnoside, myricetin 3-rutinoside, quercetine, quercetine 3-*O*-α-L-arabinofuranoside, quercetine 7-arabinoside, quercetine 3-*O*-β-L-arabinoside, quercetine 3-*O*-β-D-galactopyranoside, quercetine 3-*O*-β-D-glucopyranoside, quercetine 3-*O*-α-L-rhamnoside, quercitrin, rutin - in aerial part.[89,110,117,119-122] The flavonoid content in the aerial part ranged from 4% to 5.71%.[121,123]

Biflavonoids: 3,8'-biapigenin – in aerial part;[89,122] amentoflavone (3',8''-biapigenin), 5,5″-dihydroxy-7,4′,7″,4‴-tetramethoxybiflavone – in leaves and flowers.[119,120,124]

Catechins: (+)-catechine, (-)-epicatechine - in aerial part.[110,120,122]

Xanthones: 1,7-dihydroxyxanthone, 1,7-dihydroxy-4-methoxyxanthone, 7-epiclusianone, hyperxanthones A – F, 1,3,5,6-tetrahydroxyxanthone, 1,3,6,7-tetrahydro-8-(3-methyl-2-butenyl)-9H-xanthene-9-one, toxyloxanthone B, 1,3,7-trihydroxyxanthone - in aerial part.[89]

Anthraquinone: hypericin, pseudohypericin – in leaves and flowers.[76,83,117,119,120,125,126]

Oxygen-containing heterocycles: amylfuran (2-pentylfuran), 3,4-dimethyl-5-pentylidene-2(5*H*)-furanone, 12-norcyercene B, 4H-pyran-4-one - in aerial part.[98,105,106,109]

Nitrogen-containing heterocycles: furo[2,3-b]quinolin-4(9H)-one – in aerial part.[109]

Aliphatic hydrocarbons and derivatives: (*E,E*)-2,4-decadienal, decanol, 3,7-dimethyl-(*Z*)-1,3,6-octatriene, 3,7-dimethyl-(E)-1,3,6-octatriene, dodecanol, ethanone, heneicosane, (*E,Z*)-2,4-heptadienal, hexahydroformylacetone, hexatriacontane, hexenal, (Z)-3-hexenal, 6-methyl-3,5-heptadien-2-one, 6-methyl-5-hepten-2-ol, (*E,Z*)-2,6-nonadienal, nonanal, 2-nonanol, 3-nonanol, 2-nonanone, octadecane, (*Z,Z,Z*)-9,12,15-octadecatrien-1-ol, octanal, octanol, pentacosane, sulcatone (2-methyl-6-heptenone), tetracosane, 2-tridecanone, tricosane, *n*-undecane - in aerial part;[97,98,100,102,103,105-109] *n*-nonane - in aerial part and callus (hypocotyl explants);[96,97,100,105,106] nonacosane – in leaves, stems, and seeds;[102,103] heptadecyloxirane (1,2-epoxynonadecane) – in leaves and stems;[102,103] 6,10,14-trimethyl-2-pentadecanone – in leaves and flowers;[102,103] 1-hexadecanol, nonadecane, 2,6,10,14,18,22-tetracosahexene, tetracosanal – in leaves;[102,103] 1-dotriacontanol, hexadecane, 9-tricosane – in stems.[102]

Fatty Acids: arachidic, behenic, lignoceric, linoleic (ω-6), linolenic (ω-3), stearic - in leaves, stems, flowers, and fruits;[102,103,109,110,127] capric, caprylic, enanthic, lauric, myristic, oleic, palmitic, pelargonic, pentadecanoic - in aerial part;[98,102,103,105,106,109,110,127] cerotic, margaric – in leaves and stems;[102,103] 7- heneicosanoic, hexadecenoic, nonadecanoic – in stems;[102] 9-hexadecenoic – in leaves and flowers.[102,103,110] In hexane extracts from flowers, leaves, stems, and seeds, the predominant component (29–43.2%) was α-linolenic acid (omega-3 fatty acid), one of the essential fatty acids; the highest

concentration of ω-3 fatty acid was found in seeds (37.6%) and leaves (43.2%).[102,103]

Vitamins: retinol, δ-tocopherol, vitamin D, vitamin K – in flowers.[110]

Essential oil: in aerial part - 0,19% (Turkey);[99] 0,2% (Uzbekistan);[98] 0,96% (Iran).[128,129] The yield of essential oil and its chemical polymorphism depends on the geoecological regions of plant growth and environmental factors. Below are examples of the composition and percentage of the main components of essential oil from different regions of plant growth.

A method (*in vitro*) for growing callus from hypocotyl plant explants to obtain essential oils on an industrial scale has been developed; the material was taken from ten different wild populations (Turkey). The composition of callus essential oil was characterized by relatively high variability, and the main, most common components were recognized: α-pinene (7.68-40.20%), β-pinene (1.30-35.74%), limonene (0.02-32.21%), β-ocimene (0-37.90%) and germacrene D (0.15-30.55%).[96]

Biological Activity

Antibacterial Activity. Extracts from the aerial part (acetone, chloroform, ethanol as a solvent) exhibit different degrees of antibacterial activity against strains of *Bacillus megaterium*, *B. subtilis*, *Proteus vulgaris*, *Streptococcus pyogenes*, and *Staphylococcus aureus*.[85] An ethanol extract from the aerial part demonstrates antimicrobial properties against *Klebsiella pneumoniae*, *K. oxytoca*, *Enterobacter aerogenes*, *E. cloacae*, *Escherichia coli*, *Salmonella typhimurium*; the most significant activity was revealed against *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *S. epidermis*, and *Streptococcus pyogenes.*[133] In addition, the hydromethanolic extract significantly suppressed the growth and development of *S. aureus.*[134] In other studies, ethanol extract (the sum of phenolic compounds) exhibited a significant bacteriostatic effect against *S. aureus*, was less active against *E. coli* and *Mycobacterium tuberculosis*, and showed insignificant antibacterial properties against *Proteus vulgaris;*[135] the activity of pure compounds of flavonoids gave average results against strains of *S. aureus* and *E. coli.*[122] Hexane extracts from flowers, leaves, stems, and seeds showed moderate inhibitory activity against gram-positive (*Bacillus subtilis*, *Enterococcus faecalis*, *S. aureus*, *S. epidermidis*) gram-negative (*Escherichia coli*, *Pseudomonas aeruginosa*) bacteria; extracts from leaves and seeds showed the best results.[102,103] In experiments, an alkaline (NaOH) extract from dried flowers was active against *B. cereus, B. megaterium, B. brevis, B. subtilis var. niger, Mycobacterium smegmatus, Pseudomonas aeroginosa*, and *Yersinia enterocolitica*. Ethyl acetate extract was active against *B. megaterium* and *B. brevis*. Pyridine extract was active against *M. smegmatus* and *B. megaterium*; ethanol and methanol extracts inhibited the growth of *B. subtilis var. niger.*[136] In other experiments, a potent activity (higher than standard antibiotics) of aqueous and ethanol extracts from flowers against *B. megaterium, B. subtilis, E. coli, P. aeruginosa, K. pneumonia, P. vulgaris, S. aureus,* and *Listeria monocytogenes* were revealed.[110] The antibacterial activity of an extract from the aerial parts of the plant, containing α-pinene, thymol, and carvacrol, was investigated against four pathogens – *S. areus, P. aeroginosa, B. cereus and E. coli*; the most sensitive to the extract were the gram-negative bacteria *E. coli* and *P. aeruginosa* .[137] An ethyl acetate extract from flowers and leaves containing 5,5″-dihydroxy-7,4′,7″,4‴-tetramethoxybiflavone, was moderately active against several pathogenic bacteria (*B. subtilis*, *E. faecalis*, *S. aureus*, *S. epidermidis*, *E. coli*, *P. aeruginosa,* and *K. pneumoniae*).[124] The essential oil from flowers and fruits exhibited bacteriostatic properties against *S. aureus* and *E. coli*.[132] essential oil from flowers demonstrated significant antibacterial activity against *Bacillus cereus, Listeria monocytogenes, Proteus vulgaris,* and *Salmonella typhimurium*.[101] Other studies of essential oil from the aerial part revealed activity against strains *B. brevis, B. cereus, E. coli* (K12, PBR 322, PUC 9), *P. aeruginosa, S. aureus*, and *S. pyogenes,*[138] as well as selective activity against *Cryptococcus neoformans* and *Mycobacterium intracellulare*; the main components of the oil (α-pinene, β-pinene, and myrcene) were inactive.[130] Phloroglucinol derivatives (hyperibones A, B, C, and D) exhibited a bactericidal effect against methicillin-sensitive (MSSA) and methicillin-resistant (MRSA) *S. aureus* strains.[88] Anthraquinone hypericin has demonstrated (in vitro) photodynamic inactivation of *S. aureus, E. faecalis*, and *E. coli* microorganisms, without significant damage to human fibroblasts;[139] the photosensitizing properties of hypericin were shown experimentally on MSSA and MRSA *S. aureus* strains.[140] Experiments on nano photosynthesis of silver nanoparticles (AgNPs) by hydromethanolic extract from seeds and screening for antimicrobial activity against resistant human pathogenic bacteria (*Salmonella typhi, Escherichia coli, Streptococcus mutans, and S. aureus*) were performed. Bioanalysis revealed significant antibacterial activity of AgNPs (higher than the standard antibiotic gentamicin), and *S. aureus* and *S. mutans* were the most sensitive microorganisms.[141]

Antifungal Activity. An ethanol extract from the aerial part of the plant and isolated flavonoids showed moderate antifungal activity against *Candida albicans* strains.[122,133] Hexane extracts from flowers, leaves, stems, and seeds also showed moderate inhibitory properties against *C. albicans, Saccharomyces cerevisiae,* and *Aspergillus niger* (extracts from leaves and seeds showed the best results).[102,103] Antimicrobial activity against *C. albicans* was found in the NaOH extract from dry flowers;[136] in other experiments, a powerful activity (higher than that of standard antibiotics) of aqueous and ethanol extracts from flowers against *C. albicans* was revealed.[110] In other studies, the sum of phenolic compounds of the ethanol extract practically did not show activity against *C. Albicans*.[135] An ethyl acetate extract from flowers and leaves containing 5,5″-dihydroxy-7,4′,7″,4‴-tetramethoxybiflavone was moderately active against three pathogenic fungi (*C. albicans*, *S. cerevisiae and A. niger*).[124] The essential oil from the aerial parts has antimicrobial properties (*C. albicans*),[138] and also exhibits selective activity against *C. krusei*; the main components of the oil (α-pinene, β-pinene, myrcene) were inert.[130] Anthraquinone hypericin has demonstrated photosensitizing fungicidal properties (in vitro) on *Candida*

albicans, *C. parapsilosis*, and *C. krusei* strains, and was also active against the dermatophyte fungi *Trichophyton rubrum* and *T. mentagrophytes*.[142,143]

Antiprotozoal Activity. A methanolic extract from the aerial part was active against metronidazole-sensitive and -resistant strains of *Trichomonas vaginalis*, the causative agent of human trichomoniasis urogenital infection.[109] The essential oil from aerial parts shows antimalarial properties against *Plasmodium falciparum* strains (D6, W2); the main components of the oil (α-pinene, β-pinene, and myrcene) were inactive.[130]

Insecticidal and Larvicidal Activity. Hydrodistillate from the aerial part of the plant has larvicidal activity, causing 100% death of the larvae of the non-malarial mosquito (*Culex pipiens*, Diptera: Culicidae), as the concentration in water and the exposure time increase.[131] The essential oil from the aerial parts exhibits insignificant anti-mosquito properties against the yellow fever mosquito (*Aedes aegyptii*, Diptera: Culicidae).[130] The insecticidal effect of the essential oil was observed against leaf beetles, pests of legumes (*Bruchus dentipes*, Coleoptera: Chrysomelidae); significant mortality in adults was noted.[97] The oil has been reported to have toxic effects on the adults of the Colorado potato beetle (*Leptinotarsa decemlineata*, Coleoptera: Chrysomelidae) and the barn weevil (*Sitophilus granarius*, Coleoptera: Dryophthoridae), as well as on larvae and adults of the mediterranean flour moth (*Ephestia kuehniella*, Lepidoptera: Pyralidae).[144,145]

Hepatoprotective Activity. The protective role of essential oil in acetaminophen-induced liver damage in rats has been proven experimentally; oil can modulate induced hepatic toxicity by adjusting the parameters of oxidative stress damage to the liver.[146] In the studies performed, phloroglucinol derivatives (hyperscabrons, hyperibrins, etc.) isolated from the aerial part of the plant exhibited obvious hepatoprotective activity against D-galactosamine-induced damage to the liver cell line HL-7702 and paracetamol-induced damage to the HepG2 cell line.[112-116] In high concentrations, the extract from the aerial part has a pathological effect on liver cells.[147]

Anti-inflammatory and Antioxidant Activity Wound Healing Properties. Hydroalcoholic extracts (ethanol, methanol) from the aerial part and hexane extracts from different parts of the plant show significant antioxidant properties; the highest activity was found in hexane extracts from seeds.[85,100,102,103,133,134,148]In an experiment on male rats fed a diet high in fat, oxidative stress, learning, and memory impairment were revealed; the extract from the aerial part of the plant exhibited significant antioxidant activity and inhibited the harmful effects of a fat diet.[149] Ethanol extract effectively prevented protein oxidation in the model of bovine serum albumin.[150] The herb oil extract has a significant anti-inflammatory and wound-healing effect, is non-toxic, does not have a cumulative, sensitizing, and irritating effect.[151] In the experiment, in the case of second-degree burn wounds in rats, hydromethanolic extract exhibits antioxidant and anti-inflammatory activity, resulting in a wound-healing effect.[134] The significant antioxidant activity of the extracts is associated with the presence of flavonoids.[122] An ethyl acetate extract from flowers and leaves containing 5,5″-dihydroxy-7,4′,7″,4‴-tetramethoxybiflavone showed significant antioxidant activity.[124] Aqueous and ethanol extracts demonstrated potent antioxidant activity from flowers,[110] essential oil from flowers, and aerial parts also showed significant antioxidant properties.[100,101] The antioxidant activity of the essential oil from flowers and fruits is directly related to the content of α-pinene (70.21%) in it.[132]

Neuroprotective and Anxiolytic Activity. The effect of an ethanolic extract from the aerial part of the plant on the synaptic plasticity of the hippocampus in rats fed a high-fat diet has been studied; the results of the study confirm the neuroprotective effect of the extract (inhibition of the decrease in synaptic plasticity).[148] In experiments, the aqueous extract showed remarkable antihypoxic and antidepressant properties in three models of asphyxia, hemic and circulatory hypoxia in mice;[81] the extract exhibits anticonvulsant activity, significantly delaying the onset of pentylenetetrazole-induced seizures in mice.[93] In the conducted studies, phloroglucinol derivatives (hyperscabrons, hyperibrins) isolated from the aerial part of the plant exhibited significant neuroprotective activity against glutamate-induced toxicity in the neuroblastoma cell line (SK-N-SH);[112,113] an extract from the aerial part has shown antidepressant properties.[116] Inhalation of essential oil from the aerial part of the plant prevented spatial memory impairment in rats with amnesia induced by scopolamine, decreased anxiety and depression by reducing oxidative stress in the hippocampus and amygdala; the experiment carried out proves anxiolytic and antidepressant activity.[105-107] The effect of a hydroalcoholic extract from the aerial part of the plant on morphine withdrawal symptoms in adult male mice has been studied: injections of the extract significantly reduced and alleviated withdrawal symptoms.[152]

Antiviral Activity. In the experiment, the sum of phenolic compounds from the ethanol extract of the aerial part of the plant showed high virucidal activity against the influenza A PR / 8/34 (H0N1) virus.[64] Light-activated anthraquinone hypericin is considered an effective antiviral agent: in vitro experiments revealed a significant photodynamic inactivation of human immunodeficiency virus type 1 (HIV-1) and bovine diarrhea virus (BVDV); also found photocytotoxic properties about cancer cells.[89,153-155] However, some clinical studies have shown that high doses of hypericin can induce phototoxic skin reactions without showing antiviral activity in patients infected with the immunodeficiency virus (HIV-1) and hepatitis C virus (HCV).[156-158]

Cytotoxic and Antitumor Activity. Water and ethanolic extracts from flowers exhibit potent cytotoxic activity against the MCF-7, HCT-116, and LNCaP cancer cell lines.[110] Biologically active compounds (hyperibones, flavonoids, xanthones) isolated from the extract of the aerial part of the plant exhibit cytotoxicity against human tumor cell lines A-549 and MCF-7.[89] The methanol extract has a highly effective cytotoxic effect on the cell lines of osteosarcoma (Saos-2), cervical cancer (HeLa), and prostate cancer (DU-145),[159] as well as on cell lines of carcinoma (MCF-7), adenocarcinoma

of the lung (A-549), adenocarcinoma of the large intestine (HT-29) and hepatoblastoma (HepG2).[160] In addition, the fractions of petroleum ether and dichloromethane confirm the inductive ability to apoptosis against tumor cell lines MCF-7, A-549, HT-29, and HepG2.[161] Phloroglucinol derivatives (hyperscabrines) in the cytotoxicity bioassay confirmed the necrotic and apoptotic death of Bel-7402, HCT-8, and A-549 tumor cells.[112] Photoactivated anthraquinone hypericin reduced the viability of insulinoma cells (RIN-m5F).[162] At the same time, hypericin-mediated weakening of the cytotoxicity of some chemotherapeutic drugs has been identified, and the cytotoxicity of hypericin in the dark has not been identified.[163]

CONCLUSION

It is important to find various sources of phenolic compounds considering the pharmacological significance of these compounds, their potential therapeutic uses, and the growing interest in natural plant phenols. Wild populations of *H. scabrum* L. are potentially important sources of phenolic compounds: several biologically active secondary metabolites have been isolated from the plant, including anthraquinones, flavonoids, bioflavonoids, xanthones, phloroglucinol derivatives, and several other compounds. The extensive range of the plant and the preliminary results of a sample survey of natural resources show that the plant has a significant raw material base. The inclusion of *H. scabrum* L. in the number of pharmacopoeial species will significantly expand the harvesting potential of St. John's wort herb in the territory of the Republic of Kazakhstan, the republics of Central Asia, and the Caucasus.

Reconnaissance studies of the stock its density in some areas of Central Asia and Kazakhstan showed that the plant is found en masse in several communities and is a coedificator and dominant of herbage. In such communities, the raw materials for the aboveground part of the plant range from 30 to 110 kg per hectare.

Areas with significant participation of St. John's wort have also been identified in the grass stands of mountain steppes and juniper forests on the Hissor range (Varzob gorge, Baysun plateau), Turkestan range (Shakhristan lane, Lyangar river valley, Aburdon and Rarz villages), Qurama range (Kamchik pass), Tajik and Uzbek mountain ranges and also in the Dzungarian Alatau (Sarkand, Dzhansugurov, Koksu, Tyshkan), the Chu-Ili mountains (Kurdai pass) and the Karatau range (the Kasylusu, Boztorgai, Kantagi river valleys) of the Republic of Kazakhstan.[164-167]

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