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CHEMICAL COMPOSITION AND PHARMACOLOGICAL ACTIVITY OF PLANTS OF THE *Hypericum* L. GENUS

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ХИМИЧЕСКИЙ СОСТАВ И ФАРМАКОЛОГИЧЕСКАЯ АКТИВНОСТЬ РАСТЕНИЙ РОДА *Hypericum* L.

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Abstract. The purpose of this work was to present the results of summarizing the literature data on the chemical composition and pharmacological activity of the *Hypericum* L. genus. The chemical composition of St. John's wort (Hyperici herba) has been studied quite fully within the Eurasian area of the species; more than 80 components have been identified. The main biologically active compounds of raw materials are anthracene derivatives (hypericin), flavonoids (rutin, quercetin, hyperozoid), phenylpropanoids (chlorogenic acid) and hyperforin. The review article presents physical constants and spectroscopic ((-NMR) proton magnetic resonance, (^{13}C NMR) ^{13}C nuclear magnetic resonance, (-UV) ultraviolet, (-IR) infrared) interpretations of biologically active substances obtained from secondary metabolites from species belonging to genus. The results of pharmacognostic and pharmacological studies determine the feasibility of clinical trials of St. John's wort raw materials drugs and their use in a wide therapeutic range in the complex treatment of diseases. Herba St. John's wort is a promising source of raw materials for obtaining antibacterial, antiviral, anti-inflammatory, astringent, diuretic, antidepressant, antioxidant, anticarcinogenic, immunotropic and adaptogenic agents.

Аннотация. Целью настоящей работы явилось изложение результатов обобщения литературных сведений о химическом составе и фармакологической активности представителей рода *Hypericum* L. Химический состав зверобоя травы (Hyperici herba) изучен достаточно полно в пределах евроазиатского ареала видов, выделено более 80 компонентов. Основными биологически активными соединениями сырья являются антраценпроизводные (гиперицин), флавоноиды (рутин, кверцетин, гиперозоид), фенилпропаноиды (хлорогеновая кислота) и гиперфорин. Приведены физические константы и спектроскопические ((-ПМР) протон магнитный резонанс, (^{13}C ЯМР) ^{13}C ядерный магнитный резонанс, (-УФ) ультрафиолетовый, (-ИК) инфракрасный) интерпретации биологически активных веществ, полученных из вторичных метаболитов, от видов, принадлежащих к роду. Результаты

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фармакогностических и фармакологических исследований обусловливают целесообразность клинических испытаний препаратов зверобоя и их использования в большом терапевтическом диапазоне при комплексном лечении заболеваний. Трава зверобоя является перспективным источником сырья для получения антибактериальных, антивирусных, противовоспалительных, вяжущих, диуретических, антидепрессивных, антиоксидантных, антиканцерогенных, иммунотропных и адаптогенных средств.

Keywords: spectroscopy, flavonoids, *Hypericum*.

Ключевые слова: спектроскопия, активные вещества, флавоноиды, зверобой.

Of the 200 species distributed in the temperate subtropical and mountainous regions of tropical countries, especially in the Mediterranean, there are 27 species in the Caucasus, 13-15 species in Azerbaijan.

The following species are distributed in Azerbaijan: 1. *Hypericum androsaemum* L. 2. *H. asperuloides* Czern. & Turcz. 3. *H. atropatanum* Rzazade. 4. *H. formosissimum* Takht. 5. *H. scabrum* L. 6. *H. hirsutum* L. 7. *H. antasiaticum* Grossh. 8. *H. lydium* Boiss. 9. *H. karjaginii* Rzazade. 10. *H. polygonifolium* Rupr. 11. *H. theodorii* Woronow 12. *H. acutum* Moench. 13. *H. elegans* Steph. 14. *H. venustum* Fenzl.

Sepals and petals 5, petals twisted into inflorescences. Stamens numerous in 3 or 5 bundles, fused at the base of the filaments. The ovary is usually not completely 3-5-locular, with numerous ovules, rarely the ovary is unilocular; columns 3-5, free or fused at the base; stigmas are capitate. The flowers are yellow, numerous, in semi-umbels, paniculate or corymbose inflorescences, sometimes the flowers are solitary at the end of the stem. The fruit is a leathery capsule that cracks on the nest when ripe, rarely a single-celled or berry-like capsule. Seeds numerous, small, varied. Herbs, less often shrubs or semi-shrubs, usually with opposite sessile or short petioles with entire leaves, often with black dotted glands. [30].

The purpose of the study is to summarize information about the chemical composition, pharmacotherapeutic effect of biologically active compounds of the herb St. John's wort, genus *Hypericum* L. [30].

The composition of the species belonging to the genus is chemically rich. Species belonging to the genus contain flavonoids, anthracene derivatives, essential oils, polyphenolic compounds, etc. from secondary metabolites [4, 13, 40]. Species composition of *Hypericum coadunatum*, *H. perforatum*, *H. maculatum, H. hirsutum, H. tetrapterum* by high performance liquid chromatography, NMR nuclear magnetic resonance, (-UV) ultraviolet, (IR) infrared and mass spectroscopic analysis of a number of biologically active compounds: obtained mangiferin, avicularin, kaempferol glycoside, kaempferol rutinoside, hypercin, pseudohypercin, catechin, epicatechin, cinnamon, chlorogen, neochlorogen, vanillic acid, quercetin, rutin, bisapigenin, diquercetin, hyperoside, as well as hyperforin, β-sitosterol, estrogen, etc. [28, 36, 49]. From the species of St. John's wort *H. empetrifolium, H. sinaicum*, identified: dianthrone anthracene derivatives were hypercin, protohypercin, pseudohypercin, protopseudohypercin, cyclopseudohypercin, as well as hyperforin, adhyperforin [18, 27, 40].

The following shows some of these compounds physicochemical constants, structures, spectroscopic (UV) ultraviolet, IR-infrared, ^{1}H-NMR proton magnetic resonance, mass spectroscopic interpretations.

1. 3,8''-bisapigenin

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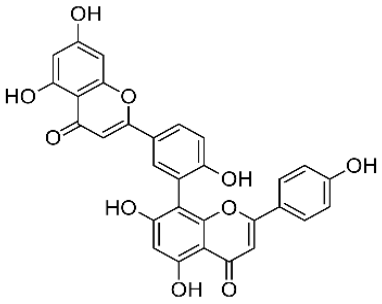
$C_{30}H_{18}O_{10,}$ m.p.= 233-235°C

M^+ 302 (100%) (UV-spectrum: (ethanol) λ_{max} =270, 330 nm) ^{1}H NMR spectrum: deuteriumacetone (acetone-d_6 (δ ppm.): 13.15 (s, 5-OH), (12.99 s, 5"-OH), 7,71 (d, J=9 Hz, 2H, H-2', 6'), 7,51 (d, J=9 Hz, 2H, H-2"', 6"'), 6,90 (d, J=9 Hz, 2H, H-3', 5') 7,79 (d, J=9 Hz, 2H, H-3"', 5"'), 6,61 (s, H-3"), 6,60 (d, 2, 5 Hz, *3,8″* –H-6), 6,34 (s. H-6") [4, 13, 28, 49].



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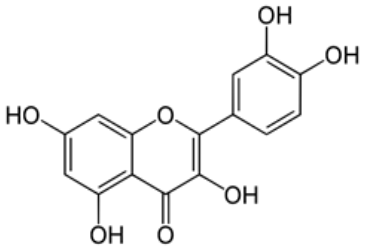
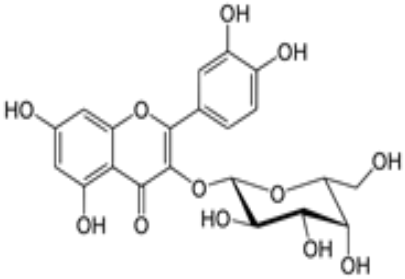
2. *quercetin*

$C_{15}H_{10}O_7$, m.p.= 312-314 °C, UV-spectrum: (ethanol) λ_{max} =257, 268, 372 nm) PMR deuteriumacetone (acetone-d6 (δ ppm.): 12,20 (s, 5-OH), 7,83 (d, J= 9 Hz, H-2'), 7,70 (dd, J_1=2, J_2=9 Hz), 6,99 (d, J= 9 Hz, H-5'), 6,53 (d, J=25 Hz, H-6) [4, 13, 28, 49].



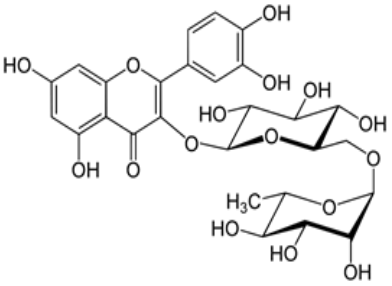
3. Hyperozide

$C_{27}H_{30}H_{16}$, m.p. = 233-235 °C, (aque:acetone), UV-spectrum: ((ethanol) λ_{max} =258, 266, 362 nm), PMR deuteriumacetone və deuteriumwater) mixture (2:1), (δ ppm.): 2.30 (s, 5-OH), 7,92 (d, J=2,5 Hz, H-2'), 7,55 (d.d, J_1=2,5, J= 9 Hz, H-6'), 6,88 (d, J= 9 Hz, H-5'), 6,45 (d, J= 2,5 Hz, H-8), 6,21 (d, J= 2,5 Hz, H-6), 5,20 (d, J= 7,5 Hs, H-1" galactosa), 3,5-3,6 m, 6 H, galactosa) [4, 13, 28, 49].



4. Rutin

$C_{27}H_{30}O_{16}$, m.p. = 192-194 °C, (water -alcohol), UV-spectrum: (ethanol)) λ_{max} =258, 266, 362 nm), ^{1}H NMR-spectrum: deuterium acetone and deuterium water mixture (2:1), (δ ppm.): 7,74 (d, J=9 Hz, H-2'), 7,68 (dd, J_1=2,5 J_2= 9 Hz, H-6'), 6,94 (d, J=9 Hz, H-5', 6,50 (d, J= 2,5 Hz, H-8), 6,27 (d, J=2,5 Hz, H-6), 5,13 (d, J= 7 Hz, H-1" -glucose), 4,55 (d, J= 2Hz, H-1"' - rhamnose), 3.70-3,25 m, 6H glucose + rutin+4H rhamnose), 1,08 (d, J= 6 Hz, 3H, CH_3 rhamnose [4, 13, 28, 49].



^{13}C NMR (100 MHz, DMSO-d_6, δ, ppm): 157.0 (C-2), 133.8 (C-3), 177.8 (C-4), 161.7 (C-5), 99.2 (C-6), 164.6 (C-7), 94.0 (C-8), 156.9 (C-9), 104.4 (C-10), 122.0 (C-1'), 115.7 (C-2'), 145.2 (C-3'), 148.9 (C-4'), 116.7 (C-5'), 121.6 (C-6'), 101.7 (C-1"'), 74.5 (C-2"), 76.9 (C-3"), 71.0 (C-4"), 76.4 (C-5"), 67.4 (C-6"), 101.2 (C-1"'), 70.8 (C-2"'), 70.5 (C-3"'), 72.3 (C-4"'), 68.7 (C-5"'), 18.2 (C-6"') [59]

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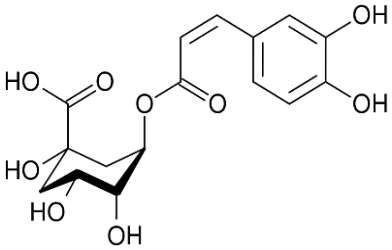
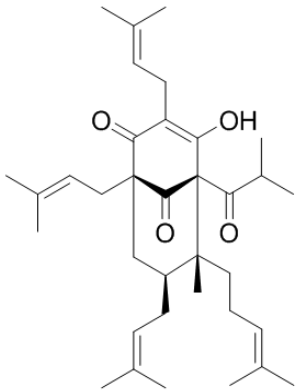
5. chlorogenic acid



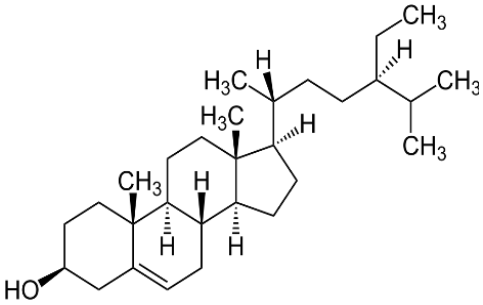
$C_{16}H_{18}O_9$, m.p.=203-205°C, (water), UV-spectrum: ((ethanol) λ_{max} =243, 300, 330 nm), ^{1}H NMR- spectrum: DMSO-d6. 100 MHz, δ ppm.), (7,45 (d, J=7,45Hz, H-7), 7,06 (d, J=2Hz, H-2'), 7,01(dd, J_1=2, J_2=8Hz H-6'), 6,80 (d, J=8Hz, H-5'), 6,18 (d, J=16 Hz H-8), 5,10 (dt, J_1=5, J_2=J_3=9Hz H-5), 4,00 (q, J=3 Hz, H-3), 3,62 (dd, J_1=3, J_2=9 Hz, H-4), ^{13}CNMR spectrum: (100 MHs, CDCl3, *chlorogenic acid* DEPT, δ: 180.2 (C-7), 168.8 (C-9'), 147.9 (C-3'), 145.6 (C-7'), 144.9 (C-4'), 126.3 (C-1'), 122.8 (C-6'), 116.6 (C-5'), 115 2(C-8'), 114.0 (C-2'),76.5 (C-1), 71.6 (C-5), 70.5 (C-3), 69.4 (C-4), 38.5 (C-2), 37.9 (C-6). [28, 49].

6. hyperforin



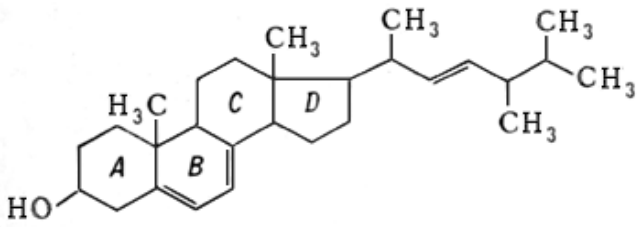
$C_{35}H_{54}O_4$, m.p..= 79-80°C, UV-spectrum: ((ethanol) λ_{max} =275 nm), ^{1}H NMR- spectrum: deuteriumchloroform $CDCl_3$ (δ ppm.): 4,8-5,3 (m, 4H, H-15, H-22, H-27, H-32), 4,2-4,3 (m 2H, H-14), 3,20 (m, 1H, H-11), 1,8-2,5 (10H, H-6, H-7, 2H-19, 2H-21, 2H-26, 2H-31), 1,5-1,8 (m, 28H, CH_3-17, 18, 24, 25, 29, 30, 34, 35), 1,20 (s, 6H, CH_3-12, CH_3-13), 1,00 (3H, CH_3-20) [4. 44. 49, 59].

7. β-sitosterin



$C_{29}H_{50}O$, m.p.= 132-133°C, ^{1}H NMR- spectrum: deuteriumchloroform CDCl3 (δ ppm.): 5,32 (m, 1H, H-6, 3,73 (m, 1H, H-3), 0,8-2,2 (m, 47H, also 6 CH_3 -də including) Mass-spectrum: (70 eV, 200°C, m/z, %), 414 (M^+ 32), 255 (32), 231 (19), 213 (27), 145 (34), 135 (37), 119 (60), 145 (34), 135 (37), 119 (60), 105(43), 97(58), 71(63), 69(65), 43(50). IR-spectrum: (ν_{max} cm^{-1}) OH group (3450-3345), 1500, 1450 (C=C) [49].

8. Ergosterin



$C_{28}H_{44}O$, ə.t.=163-165°C, (UV-spectrum: (ethanol) λ_{max} =271 nm)), $[a]_D$-129°, ^{1}H NMR-spectrum: deuteriumchloroform CDCl3 200 MHs (δ m.h.): 5,35 (m, 2H, H-6, H-7), 4,37 (d, 2H, H-22, H-23), (m, 1H, H-3), 3,1-3,4 (m, 2H, H-9, H-24), 0,65-2,4 (m, 47H, also 6 CH_3), mass spectrum: (70 eV, 200°C, m/z, %), 396 (M^+, 100), 255 (7), 213 (13), 147 (28), 80 (34), 57 (52), 43 (68) [49].

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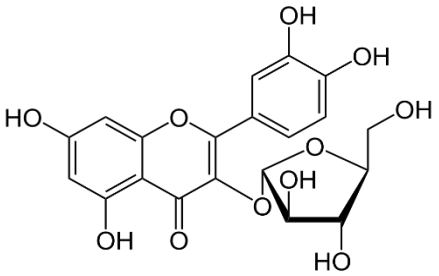
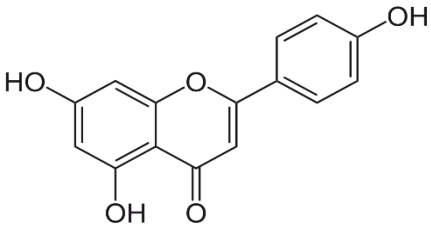
9. Avicularin (guajavarin), (quercetin-3-O-α-L-arabinofuranoside)



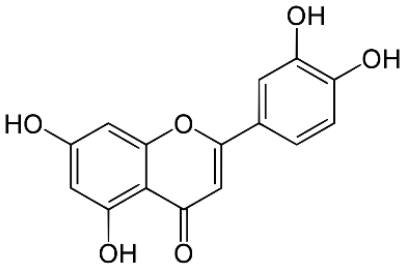
$C_{20}H_{18}O_{11}$, MALDI-TOF-MS m/z: 457 $[M+Na]^+$, 435 $[M+H]^+$.PMR (600 MHz, CD_3OD, (δ m.h.),(J Hz): 3.49-4.33 (5H, m, Ara-H-2-5), 5.48 (1H, s, Ara-H-1), 6,24 (1H, d, J=1.5, H-6), 6.42 (1H, d, J=1.5 H-8), 6.93 (1H, d, J=7.9, H-5'), 7.52 (1H, dd, J=2.1, 7.9, H-6'), 7,56 (1H, d, J=2.1, H-2'). ^{13}C NMR (125 MHz, CDOD3, δ, ppm): 62.55 (Ara-C-5), 78.66 (Ara-C-3), 83.38 (Ara-C-2), 88.04 (Ara-C-4) 93.36 (C-8), 98.48 (C-6), 104.22 (C-10), 109.67 (Ara-C-1), 115.04 (C-2'), 115.43 (C-5'), 121.57 (C-1'), 121.88 (C-6'), 133.51 (C-3), 144.96 (C-3'), 148.45 (C-4'), 157.17 (C-9), 157.96 (C-2), 161.64 (C-7), 178.60 (C-4) [13, 15].

10. apigenin



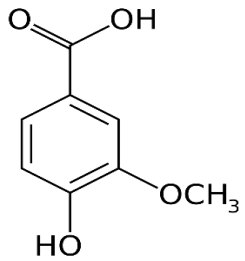
$C_{15}H_{10}O_5$ (5,7,4') trihydroksyflavone) m.p.=343-346°C, UV-spectrum: (ethanol) λ_{max} =272, 343 nm) + CH_3COONa 275, 365;+ $CH_3COONa+H_3BO_3$ 272, 345, (İQ-) spectrum (KBr, ν_{max}, cm^{-1}): 3520-3100 (OH), 1665-1635) (C=O ɣ-pyrone), 1625-1440 cm^{-1} (aromatic cycle double bonds) [1, 13]

11. Luteolin (5,7,3',4'-tetrahydroksyflavone)



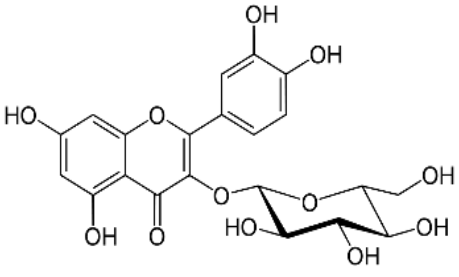
$C_{15}H_{10}O_6$ m.p..= 328-330°C, UV-spectrum: (etanol, λ_{max} , nm:) = 260, 272, 356) + CH_3COONa 272, 368; + $CH_3COONa+H_3BO_3$ 272, 376. IR-spectrum: (KBr, ν_{max} , cm^{-1}): 3450-3300 (OH), 1665-1635 (C=O ɣ-pyrone, 1612-1580 aromatic cycle double bonds), PMR (100 MHz, C_5D_5N, (δ m.h.),(J Hz): 6.61 (1H, d, J=2.0 H-6), 6.73 (1H, d, J=2.0, H-8), 6.78 (1H, s, H-3), 7,09 (1H, d, J=8.0, H-5'), 7.53 (1H, br. s, H-2'), 7.60 (1H, dd, J=2.0 və J=8.0, H-6) [13, 35].

12. Vanilic acid



$C_8H_8O_4$ m.p.=204-206°C, PMR spectrum (600 MHz DMSO-d_6, (δ ppm.),(J Hz): 7.42 (1H, s, H-2), 7.43 (1H, d, J=7.6, H-6), 6.82 (1H, d, J=7.8, H-5), 3.8 (3H, s, 3-OCH_3). ^{13}C NMR spectrum: DMSO-d6, (δ ppm.): 122.6 (C-1), 112.6 (C-2), 147.1 (C-3), 151.0 (C-4), 114.9 (C-5), 123.4 (C-6), 55.5 (3-OCH_3), 166.8 (C-1') [4, 13. 16].

13. Isoquercetin



$C_{21}H_{21}O_{12}$ 465.1003, 303$[M-162]^+$. PMR (500MHz, CD_3OD, δ, ppm, J/Hz): 7.70 (d, J=2.0, H-2'), 7.57 (dd, J=2.0, 8.3, H-6'), 6.86 (d, J=8.3, H-5'), 6.38 (d, J=2.0, H-8), 6.19 (d, J=2.0, H-6), 5.23 (d, J=7.8, H-1''), 3.70 (dd, J=2.4, 11.7, H-6'), 3.57 (dd, J=5.4, 11.7, H-6''), 3.47 (dd, J=7.8, 8.8, H-2'') 3.42 (t, J=8.8, H-3''), 3.34 (dd, J=8.8, 9.3, H-4''), 3.21

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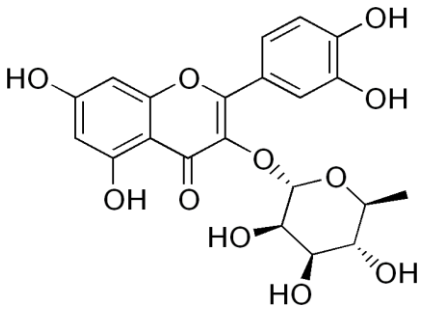
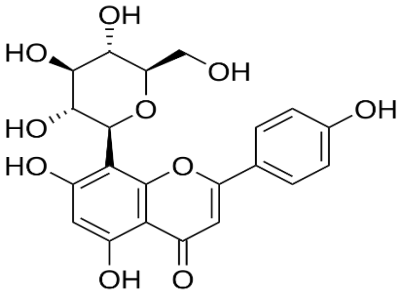
(ddd, J=2.4, 5.4, 9.3, H-5"). ^{13}C NMR (125 MHz,δ): 179.5 (C-4), 166.1 (C-7), 163.0 (C-5), 159.0 (C-2), 158.4 (C-9), 149.8 (C-4'), 145.9 (C-3'), 135.6 (C-3), 123.2 (C-12), 123.1 (C-6'), 117.6 (C-5'), 116.0 (C-2'), 105.6 (C-10), 104.4 (C-1"), 99.9 (C-6), 94.8 (C-8), 78.3 (C-5"), 78.1 (C-3"), 75.7 (C-2"), 71.2 (C-4"), 62.6 (C-6") [1, 4, 9].

14. Quercetrin 3-O-α-rhamnoside (quercitrin)



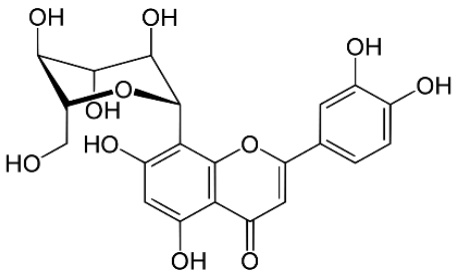
HR-ESI-TOF-MS m/z 449.1061 $[M+H]^+$ $C_{21}H_{21}O_{12}$ 449.1084, 303$[M-162]^+$, PMR (500 MHz, CD3OD, δ, ppm, J/Hz): 7.33 (d, J= 1.5, H-2'), 7.30 (dd, J=8.3, H-5, 8.3, H-6'), 6.90 (d, J=8.3, H-5'), 6.36 (br.s, H-8), 6.20 (br.s, H-6), 5.35 (br. s, H-1"), 4.21 (br.s, H-2"), 3.74 (dd, J=2.9, 9.3 H-3"), 3.41 (m, H-5"), 3.30 (m, H-4"), 0.93 (3H, d, J=5.9, H-6"). ^{13}C NMR(125 MHz): 179.7 (C-4), 165.8 (C-7), 163.2 (C-5), 159.3 (C-2), 158.5 (C-9), 149.8 (C-4'), 146.4 (C-3'), 136.2 (C-3), 123.0 (C-1'), 122.9 (C-6'), 117.0 (C-2'), 116.4 (C-5'), 105.9 (C-10), 103.6 (C-1"), 99.8 (C-6), 94.7 (C-8), 73.3 (C-4"), 72.1 (C-3"). 72.0 (C-2"), 71.9 (C-5"), 17.6 (C-6") [4; 12].

15. *Apigenin-8-C-β-D-glucopyranoside (vitexin)*



Yellow amorphous powder, m. p. 265-66, MeOH: EtOAc (Lit. [9] m.p. 269-270°, HRESI-MS, m/z 431.0984, (calcd for $C_{21}H_{19}O_{10}$, 431.0978) [M-1]+ IR (KBr, ν_{max}, cm^{-1}), 3378, 3251, 1661, 1508. DMSO-d_6, δ, ppm, J/Hz): 6.71 (1H, s, H-3), 6.21 (1H, s, H-6), 7.98 (2H, d, J=8.8, H-2, H-6'), 6.68 (2H, d, J=8.8, H-3, H-5'), 4.73 (1H, d, J=9.8, H-1"), 3.79 (1H, d, H-2), 3.28 (1H, dd, H-3"), 3.46 (1H, t, H-4"), 3.25 (1H, d, H-5"), 3.74 (1H, dd, J=11.9, 5.8, H-6" a), 3.53 (1H, dd, J= 11.9, 2.4, H-6"b)^{13}C NMR (400 MHs, DMSO-d_6, δ): 163.85 (C-2), 102.44 (C-3), 182.01 (C-4), 156.01 (C-5), 98.35 (C-6), 163.29 (C-7), 104.62 (C-8), 161.23 (C-9), 104.64 (C-10), 121.62 (C-1'), 128.93 (C-6'), 73.46 (C-1"), 79.91 (C-2"), 78.71 (C-3"), 70.55 (C-4"), 81.82 (C-5"), 61.30 (C-6") [29, 56].

16. Luteolin-8-C-β-D-glucopyranoside (orientin)



Yellow powder, m.p. MeOH: EtOAc, m.p. 265-267°C, HRESI-MS, m/z 471.0904, (calcd for $C_{21}H_{20}O_{11}Na$, 471.0903) [M+Na]+ (100%). Optical Rotation $[a]^{20}{}_D$ +18.4 (c, 1.4 in Py), IR (KBr, ν_{max}, cm^{-1}), 3246 (ν_{O-H}), 1655 ($\nu_{C=O}$), 1614, 1508, 1428 (δ_{C-H}); PMR (200 MHs, DMSO-d_6, ppm,δ, J/Hz): 13.17 (s.OH-5), 7.50 (1H,dd, J_1=8.0, J_2=2.1, H-6) 7.44 (1H, d, J=2.1, H-2), 6.90 (1H, d, J=8.2, H-5'), 6.65 (1H, s, H-3), 6.25 (1H, s, H-6), 4.72 (1H, d, J=9.4, H-1"), 3.82 (1H, t, J=9.4, H-2"), 3.24 (1H, m, H-3"), 3.37 (1H, t, J=9.4, H-4"), 3.21 (1H, m, H-5"), 3.75 (2H, m, H-6"). ^{13}C NMR (50.3 MHz, DMSO-d_6, δ): 164.2 (C-2), 102.4 (C-3), 182.0

(C-4), 160.5 (C-5), 98.3 (C-6), 162.8 (C-7), 104.6 (C-8), 156.0 (C-9), 103.9 (C-10), 121.9 (C-1), 114.1 (C-2'), 145.9 (C-3'), 149.9 (C-4'), 115.8 (C-5'), 119.4 (C-6'), 73.5 (C-1"), 70.9 (C-2"), 78.9 (C-3"), 70.8 (C-4"), 82.0 (C-5"), 61.8 (C-6") [29, 56].

Pharmachologic effect

Due to the uncontrolled and widespread use of antimicrobial drugs, the problem of microbial resistance to them has arisen. In this regard, it is important to use low-toxic and well-tolerated herbal preparations of St. John's wort from benign raw materials with established active substances that, in addition to antimicrobial action, also exhibit immunotropic, antioxidant and adaptogenic activity in the complex therapy of various diseases. The herb *H. perforatum and H. maculatum* has been widely used in folk medicine for the treatment of "ninety-nine diseases" since ancient times in Russia and Eurasia [22, 41].

The chemical composition of St. John's wort is currently studied quite fully. In different parts of the aerial parts of plants, more than 80 components [17] from the groups of biologically active compounds (BAS) with different pharmacotherapeutic effects have been isolated.

In general, phenolic compounds with a wide spectrum of action, including antioxidant and anticarcinogenic activity, are of pharmacological interest in St. John's wort. Preparations based on them are used in clinical practice as antimicrobial, anti-inflammatory, choleretic, diuretic, hypotensive, astringent, laxative, tonic and adaptogenic agents in complex therapy [8, 19, 32, 39, 44, 54, 57, 59, 63].

A wide range of phenolic compounds has been isolated in St. John's wort. The main BAS of St. John's wort are photoactive condensed anthracene derivatives of the quinoid structure and their glycosides (anthraquinones): hypericin, a red fluorescent pigment, protohypericin, pseudohypericin [10, 11, 37].

Use in the treatment of diseases of the skin and mucous membranes

1% spirit solution of "Novoimanin" drug is used as an inhalation for infected wounds, burns, pyodermatitis, pharyngitis and sinusitis, diseases of the oral cavity: periodontitis, gum diseases, as well as tuberculosis, laryngitis [3, 20, 61].

Total phenolic content, antioxidant activity, and the main constituents of three *Hypericum* species (*H. perforatum, H. scabrum, and H. origanifolium*) from Turkey had been investigated in this study. The quantification of main constituents (hypericin, and pseudohypericin) was performed by HPLC. The aerial parts of the plant extracts were screened in terms of their total phenolic content (TPC) and antioxidant activity tests including DPPH (2,2 diphenyl 1- picrylhdrazyl) radical scavenging activity, trolox equivalent antioxidant capacity (TEAC), ferric cyanide reducing (FRAP) antioxidant power assay, and total antioxidant activity by ferricthiocyanate (FTC).

The highest TPC value (148.31 ± 4.57 mg GAE/g DW) was obtained for H. scabrum (HS) while H. perforatum (HP) extract had the highest hypericin (9.57 ± 0.07 µg/mL), and pseudohypericin (7.82 ± 0.05 µg/mL) amount.

All Hypericum species demonstrated stronger DPPH activities than the standard compounds butylated hydroxytoluene (BHT) and ascorbic acid (AA) with the values of IC_{50} < 3.8 µg/mL. The highest trolox equivalent antioxidant capacity (TEAC) value (11.28 ± 0.28) was achieved with HO. Considerable values were obtained for HS (90.25 ± 0.05), HP (90.20 ± 0.07), and HO (88.42 ± 0.02) by total antioxidant determination using ferricthiocyanate (FTC) method with 2 days incubation. This study reveals that all Hypericum species are good sources of natural antioxidants with high TPC and major constituent contents [52].

Use in diseases of the gastrointestinal tract and liver

In clinical trials, the preparations gave a positive result: microclyzes - for post-dysenteric colitis, dysbacteriosis [48, 60], tinctures - for chronic gastritis; they increase bile outflow, restore normal peristalsis, and improve venous outflow [53. 62]. The infusion has hepatoprotective properties [21, 47]. Dry extract "Sibektan" is used as a choleretic and hepatoprotective agent [7, 33].

The tincture is used in the clinic as an additional remedy for the treatment of diabetes mellitus [24, 50]. The herb is a part of antidiabetic preparations (Arfazetin, Brusniver, Lydia 1, 2, 3 [50], Mirfazin [38]), which have diuretic, antimicrobial and anti-inflammatory effects. The tincture is used in clinical practice for the treatment of urological diseases: nephritis, cystourethritis; after urological operations as an anti-inflammatory agent; drugs have a diuretic effect [2, 5, 34, 55].

On the basis of the Bashkir State Medical University, an experimental batch of foaming vaginal tablets with dry St. John's wort polyextract was produced for use in gynecological practice [17].

St. John's wort preparations in Russia have long been used as a sedative [41], at present, interest in them as antidepressants is being updated. They have sedative and antidepressant properties due to hypericin and hyperforin [58], increase the adaptation of the psycho-emotional sphere, and have a calming effect on the cardiovascular system, which is confirmed by meta-analyzes. The drugs are used as an auxiliary antidepressant for behavior correction, treatment of mild depressive conditions and insomnia, they are more safe and tolerable [11, 23, 31, 37, 57, 63]. Herbal extracts used in complex therapy: Gelarium Hypericum [14], Deprim, St. John's wort, Negrustin, Trioson, Yarsin 300, etc. [6, 7, 49]. Preparations based on St. John's wort, including essential oil, are active against penicillin-resistant staphylococcus, streptococcus, salmonella, and shigella [25. 42, 45]. Volatile fractions and juice have protistocidal and bacteriostatic properties [24, 34]. The active substances of St. John's wort are active against influenza, herpes, hepatitis B viruses [43, 46, 51], hypericins — against HIV [39].

In the experiment (rats, mice), the aqueous extract had radioprophylactic and radiotherapeutic properties, protected the bone marrow and small intestine from radiation damage [8, 32, 54]. The mechanisms of the antitumor effects of *Hypericum perforatum* L. (St. John’s wort, SJW) and its main active component hyperforin (HPF). SJW extract is commonly employed as antidepressant due to its ability to inhibit monoamine neurotransmitters re-uptake. Moreover, further biological properties make this vegetal extract very suitable for both prevention and treatment of several diseases, including cancer. Regular use of SJW reduces colorectal cancer risk in humans and prevents genotoxic effects of carcinogens in animal models. In established cancer, SJW and HPF can still exert therapeutic effects by their ability to downregulate inflammatory mediators and inhibit pro-survival kinases, angiogenic factors and extracellular matrix proteases, thereby counteracting tumor growth and spread. Remarkably, the mechanisms of action of SJW and HPF include their ability to decrease ROS production and restore pH imbalance in tumor cells. The SJW component HPF, due to its high lipophilicity and mild acidity, accumulates in membranes and acts as a protonophore that hinders inner mitochondrial membrane hyperpolarization, inhibiting mitochondrial ROS generation and consequently tumor cell proliferation. At the plasma membrane level, HPF prevents cytosol alkalization and extracellular acidification by allowing protons to re-enter the cells. These effects can revert or at least attenuate cancer cell phenotype, contributing to hamper proliferation, neo-angiogenesis and metastatic dissemination. Furthermore, several studies report that in tumor cells SJW and HPF, mainly at high concentrations, induce the mitochondrial apoptosis pathway, likely by collapsing the mitochondrial membrane potential. Based on these mechanisms, we highlight the SJW/HPF remarkable potentiality in cancer prevention and treatment [44]. Glioblastoma is the most common primary brain tumor with poor survival rate and without effective treatment strategy. Notably, amplification and active mutation of epidermal growth factor receptor (EGFR) occur

frequently in glioblastoma patient that may be a potential treatment target. Several studies indicated that various type of herbal compounds not only regulate anti-depressant effect but also shown capacity to suppress glioblastoma growth via inducing apoptosis and inhibiting oncogene signaling transduction. Hyperforin, an herb compound derived from St. John's wort was used to treat depressive disorder by inhibiting neuronal reuptake of several neurotransmitters. Although hyperforin can reduce matrix metallopeptidases-2 (MMPs) and -9-mediated metastasis of glioblastoma, the detail mechanism of hyperforin on glioblastoma is remaining unclear. Here, we suggested that hyperforin may induce extrinsic/intrinsic apoptosis and suppress anti-apoptotic related proteins expression of glioblastoma. We also indicated that hyperforin-mediated anti-apoptotic potential of glioblastoma was correlated to inactivation of EGFR/extracellular signal-regulated kinases (ERK)/nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB) signaling [19, 44].

The review article presents information on the chemical composition, spectroscopic interpretation and pharmacological action of plants belonging to the genus St. John's wort. The main biologically active compounds of raw materials are plant pigments: anthracene derivatives of anthraquinones (hypericin, pseudohypericin) and flavonoids (rutin, bisapigenin, quercetin, apigenin, luteolin), phenylpropanoids (vanilla acid-chlorogenic acid) and phloroglucinum hyperforin, which have a wide range of pharmacological action. Of these, the active substances hypericin, hyperforin and hyperozoid (hyperin, or quercetin galactoside) are identified with the name of the plant *Hypericum* in which they are produced, which characterizes the genus specificity of the popular medicinal plant St. John's wort.

The results of modern pharmacognostic and pharmacological studies of Hyperici herba determine the feasibility of clinical trials of preparations based on St. John's wort and their use in a wide therapeutic range in complex treatment. St. John's wort is a promising source of raw materials for obtaining antibacterial, clinical and preventive medicine 29 antiviral, anti-inflammatory, astringent, diuretic, antidepressant, antioxidant, anticarcinogenic, immunotropic and adaptogenic agents.

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