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Composition of biologically active compounds, biological and pharmacological activity of the three-part beggarticks (*Bidens tripartita* L.)

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Abstract :
This review contains the analysis data on phytochemical composition of three-part beggarticks (*Bidens tripartita* L.) and full biological activity spectrum of the medicinal raw material. Flavonoids, essential oils, phenolcarboxylic acids, polysaccharides, aromatic hydroxy aldehydes, coumarins, tannins, and polyacetylenes are biologically active substances (BAS) of *B. tripartita.* Various BAS cause multiple pharmacological and biological effects of the plant. Extracts possess antimycotic, antiinflammatory, antithrombotic, antiradical, antioxidant, antibacterial, antidiabetic, antiulcerogenic, and antitumor effects. The extracts are also of analgesic, antipyretic, antiallergic, hepatoprotective, immunostimulating, and hypotensive pharmacological effects. There is also a possibility to inhibit the main enzymes as well as to protect DNA. The *B. tripartita* medicinal raw material is of great importance for development and making of new drugs.

Key words: *B. tripartita*, flavonoids, ethereal oils, polyacetylenes, phenol compounds, polysaccharides, biological activity, pharmacological activity

INTRODUCTION:

B. tripartita (the *Asteraceae L.* family) is an annual plant 30-100 cm height with yellow flowers (Fig.1).1 There are about 230 varieties of *B. tripartita* all around the world mainly in tropical and temperate zones.2 It is annual herbaceous plant that can be cultivated. *B. tripartita* usually grows near brooks, in vegetable gardens, near swamps and rivers and it is widespread everywhere.

Figure 1: *Bidens tripartita* L.3 ;

Chemical composition ;

According to extensive phytochemical research on the *B. tripartita* herb gathered in Bielsk Podlaski (Poland), biologically active compounds (BAS) composition includes flavonoids, coumarins, ethereal oil, polysaccharides, carotenoids, lactones, amines, and minerals. There are triterpenes, unsaturated aliphatic hydrocarbons, fatty acid and sterol ethers mostly consisting of stigmasterol in the *B. tripartita* petroleum extract.[4,5,6,7,8,9,10,11]

A recent phytochemical analysis of the *B. tripartita* herb has confirmed that it also includes flavonoids, polysaccharides, carotenoids, amines, lactones, minerals, coumarins, and ethereal oils. Antioxidant properties may be performed by three flavonoids: flavanomarein, cynaroside, and luteolin.[12]

According to phytochemical research on the *B. tripartita* herb gathered in Bielsk Podlaski (Poland), composition includes flavones, flavanones, chalcones, aurons, coumarins, low level of vitamin C, carotenoids, and ethereal oil. Green parts of *B. tripartita* includes polyacetylene compounds, linoleic acid, and ocimene, whereas flowers include thiophene, kosmen trails, and eugenol.[13]

According to phytochemical research and quantitative and qualitative analysis of the samples gathered in Mikkeli (Finland) and in Leningrad region (Russia), there are flavonoids, tannins, polysaccharides, phenols, amino acids, ascorbic acid, organic acids, and polyacetylenes in *B. tripartita*.1

A group of scientists from the Xinjiang Medical University (Lv and Zhang) studied chemical composition of *B. tripartita* and extracted 14 flavonoids and 2 polyacetylenes from above-ground parts of the samples gathered in July on the Wanxian mountain, Hui region, Henan province (China). Besides, according to the other *B. tripartita* phytochemical research, the herb includes flavones, flavanones, chalcones, aurons, coumarins, carotenoid, and volatile compounds.[14]

According to reports, *B. tripartita* includes significant amount of phenol compounds, flavonoids, chalcones, and aurons[15,16], coumarins[16], tannins[17], phenol acids[16], and carbohydrates including neutral and acid polysaccharides and pectin7,[18]. According to the phytochemical research on *B. tripartita*, there is small amount of vitamin C, carotenoids, and ethereal oil.[10] Green parts of *B. tripartita* contain polyacetylene compounds, linoleic acid, and ocimene, whereas flowers contain thiophene, kosmen trails, and eugenol.1,[15]

Phytochemical analysis of samples gathered in Mikkeli (Finland) and in Leningrad region (Russia): flavonoids (rutin), coumarin (phenol compound), tannins, general phenol compounds, (gallic acid), polysaccharides, amino acids (arginine equivalents), ascorbic acid, and polyacetylenes.1 The sample, gathered in Mikkeli (Finland) in August, contains mostly flavonoids, tannins, polysaccharides, and ascorbic acid. The sample, gathered in Leningrad region (Russia), contains mostly coumarins and amino acids.1 *B. tripartita* also includes coumarins, triterpenes, and ethereal oils causing antiinflammatory effect of the herb.1 A group of researchers confirms that climatic factors and geography also may cause observed differences between analysis results of the *B. tripartita* extracts.[19,20]

It is established that flavonoids, polysaccharides, and ascorbic acid are dominating groups of components containing in the *B. tripartita* samples gathered in Mikkeli (Finland), and coumarins and amino acids are dominating groups of components containing in the *B. tripartita* samples gathered in Leningrad region (table 1).1

It is found that green parts of the *B. tripartita* samples gathered in Bielsk Podlaski (Poland) contained polyacetylene compounds, linoleic acid, and ocimene. Antioxidant effect of herbal, flower, and pure flavonoids extracts: flavanomarein (izookanin-7-O-glucoside), cynaroside (7-O-luteolin glucoside), and luteolin.4,[15] Based on the quantity HPLC analysis, cynaroside is dominating flavonoid containing in the *B. tripartita* herb, and flavanomarein is dominating flavonoid containing in the *B. tripartita* flower heads.4

Antioxidant activity of pure flavonoids: flavanomarein (izookanin 7-O-glucoside), cynaroside (luteolin 7-O-glucoside), and luteolin.[13] Such pure flavonoids as zookanin 7-O-glucoside, luteolin 7-O-glucoside, and luteolin are extracted from *B. tripartita* herb gathered in Bielsk Podlaski (Poland).[13]

Izookanin and luteolin 7-O-glucosides are the main flavonoids containing in the extracts. Flavanomarein contains mostly in flowers; cynaroside contains mostly in green parts of the plant. Amount of flavonoids is calculated by Christ-Muller basing on quercetin and hyperoside.[13]

Chlorogenic acid, luteolin-7-O-glycoside (cynaroside), and luteolin dominate above all researched flavonoids and phenols.[14]

According to the literature data, the *B. tripartita* genus may be considered as a reach flavonoid source.[20] Flavones (luteolin and luteolin derivatives) and such flavanone as 7-O-glucoside-izookanin are the main phenol compounds containing in the *B. tripartita* samples gathered in August in Mikkeli (Finland).[13]

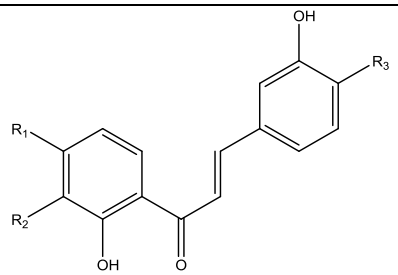
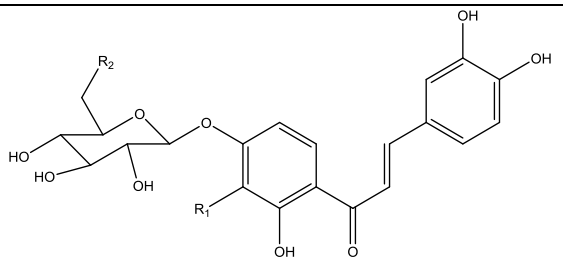
It is proved, that the *B. tripartita* samples, gathered on the bank of the Yenichaga lake, Bolu (Turkey) in late August, include chlorogenic acid, cynaroside, and luteolin.[14]

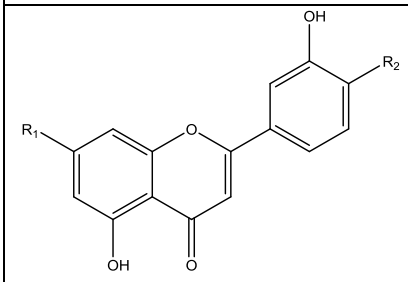
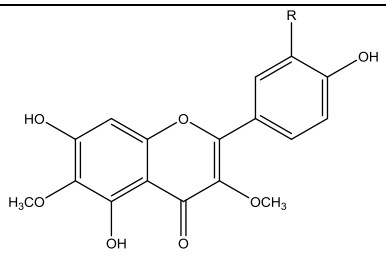
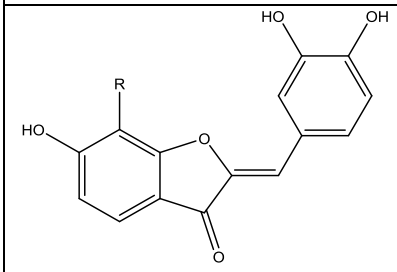
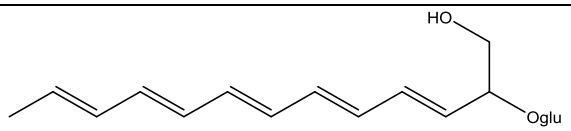
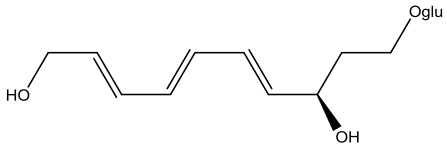
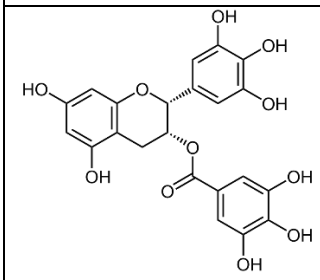
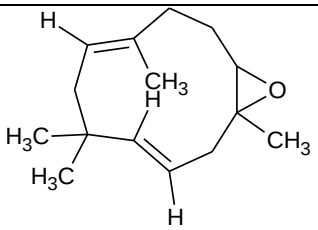
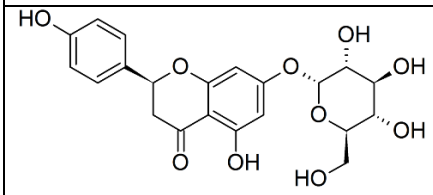
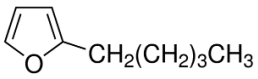
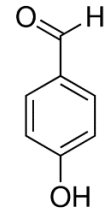
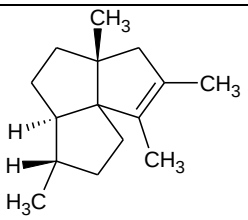
Methanol extract includes more general phenol (84.24 mgGAE/g of extract) and flavonoid (49.00 mgRE/g of extract) than ethyl acelate extract (56.64 mgGAE/g of extract and 30.10 mgRE/g of extract) and aqueous extract (50.95 mgGAE/g extract and 10.74 mgRE/g extract) containing in the *B. Tripartita* samples, gathered in Afyon (Turkey) during summer.[20]

Luteolin-7-O-glucoside (also well-known as cynaroside), chlorogenic acid, and epicatechin are the main compounds, containing in samples of the *B. Tripartita* extract, gathered in Afyon (Turkey) during summer.[20]According to a paper of Orhan et al. (2016)[14], chlorogenic acid, luteolin-7-glycoside, and luteolin are dominating phenol compounds containing in the *B. tripartita* extract and subextract. According to another research Wolniak et al. (2007)[13], luteolin-7-glucoside is also a dominating component of *B. tripartita*.[20]

It is discovered that the samples gathered in Mikkeli (Finland) and in Leningrad region (Russia) contain the following components: (+-)-catechin, chlorogenic acid, caffeic acid, luteolin-7-O-glucoside, chicor acid, rosmarinic acid, and luteolin.1 All extracts contain hydroxycinnamic acids, luteolin glycoside, and polyacetylenes (Fig. 1).1 During researching *B. tripartita* samples gathered in Finland in August, the next compounds are found: flavonoids, coumarins, tannin, general phenol compounds, polysaccharides, amino acids, ascorbic acid, (+-)-catechin, chlorogenic acid, caffeic acid, luteolin-7-O-glycoside, chicor acid, rosmarinic acid, and luteolin.1 14 flavonoids and two polyacetylenes are extracted from above-ground of *B. tripartita*.2[,20] According to the works of a group of scientists from the Xinjiang Medical University, Jie Li Lv and Lai Bin Zhang, above-ground parts of *B. tripartita* samples gathered on the Wanxian mountain, Hui region, Henan province (China) extract fourteen flavonoids and two polyacetylenes.2

Table 1: Structure formulas of chemical compounds of *Bidens tripartita* L.

 Butein: $R_1 = R_3 = OH$, $R_2 = H$ 3,20,40-trihydroxy-4-methoxychalcone: R_1 = OH, R_2 = H, $R_3 = OCH_3$	 Okanin 40-O-b-D-glucopyranoside: $R_1 = R_2 = OH$ Okanin 40-O-(600-O-acetyl-b-D-glucopyranoside): $R_1 = OH$, $R_2 = OAc$ Bidenoside G: $R_1 = H$, $R_2 = OAc$

40-O-b-D-glucopyranosyl-20,3-dihydroxy-4-methoxychalcone: R_1 = Oglu, R_2 = H, R_3 = OCH_3 Okanin: R_1 = R_2 = R_3 = OH	
 Luteolin: R_1 = R_2 = OH Diosmetin: R_1 = OH, R_2 = OCH_3 Luteoside: R_1 = Oglu, R_2 = OH	 Axillarin: R = OH Quercetagetin 3,6,30-trimethyl ether: R = OCH_3
 Sulfuretin: R = H 6,7,30,40-tetrahydroxyaurone: R = OH	 2-b-D-glycopyrasyloxy-1-hydroxytrideca-3,5,7,9,11-pentayne  3(R),8(E)-8-decene-4,6-diyne-3,10-dihydroxy-1-O-b-D-glucopyranoside
 epigallocatechin gallate	 humulene epoxide II
 naringenin-7-O-glucoside	 2-pentylfuran
 4-Hydroxybenzaldehyde	 silphiperfol-6-ene

Their structures are identified as butein, 3.20.40-threehydroxy-4-methoxychalcone, 40-O-b-D-glucopyranosyl-20.3-dihydroxy-4-methoxychalcone, okanin, okanin 40-O-(40-O-acetyl-b-D-glucopyranoside), okanin 40-O-(600-O-acetyl-b-D-glucopyranoside), bidenoside G, luteolin, diosmetin, luteoside, axillarin, 3.6.30-quercetagetin trimethyl ether, sulfuretin, 6.7.30.40-tetrahydroxyauron, 2-b-D-glycopyrasyloxy-1-hydroxytrideka-3.5.7.9.11-pentain, and 3(R), 8(E)-8-decene-4.6-diin-3.10-dihydroxy-1-O-b-D-glucopyranoside.2

Scientists Sagdic et al. (2011)[21] and Wojdyło et al. (2007)[22] extracted the following phenol components from methanol, ethyl acelate, and aqueous *B. tripartita* extracts: flavonoids (naringenin-7-glucoside, luteolin-7-glucoside, flavone, rutin, quercetin), tannins, ellagic acid, epicatechin, epigallocatechin gallate, catechin hydrate, gallic acid, hydroxycinnamic acid, phenolcarboxylic acid (neochlorogenic acid, п-hydroxybenzoic acid, gentisic acid, vanilic acid, syringic acid, salicylic acid, 4-O-caffeoylquinic acid, rosmarinic acid, caffeic acid, ferulic acid, coumaric acid, chlorogenic acid), aromatic hydroxy aldehyde (4-hydroxybenzaldehyde).[20]

These compounds might be divided into the following groups: flavonoids (naringenin-7-glucoside, etc.), tannins (catechin hydrate, etc.), and phenolcarboxylic acids (neochlorogenic acid, etc.). Luteolin-7-O-glucopyranoside is the main component of *B. tripartita*, *Bidens frondosa*, and *Bidens radiata* extracts prepared in Grodno and Vitebsk regions, where it is usually grows in July-August 2012.[23]

Luteolin-7-O -glucopyranoside (cynaroside) is the main component of the *B. tripartita* herb alcohol extract.[23] Luteolin and luteolin glycosides are also discovered in the *B. tripartita* herb alcohol extract.[23] Aurons are also identified.[23] 20% of contents of the *B. tripartita* herb extract compounds are hydroxycinnamic acids such as caffeic and quinic acid derivatives as well as unreplaced chalcones and the chalcones including hydroxyl radicals, which positions are 3’ and 4’.[23] Upon analysis of the *B. tripartita* herb alcohol extract, two polyacetylenes are discovered.[23]

To analyze polysaccharides, a 10.0 g sample of raw material is boiled in 100 ml of water with a reflux condenser for 30 minutes to filter at once. That procedure is done for four times. The extracts are mixed, vaporized in vacuum to a level of 10 ml, and mixed with 45 ml of ethanol. In 30 minutes, a sediment is centrifuged, cleaned with 50 ml of ethanol, pressed by hand, and lyophilized. Contents polysaccharide is defined by gravimetry in mg/g of dry solid matter.1

Ethereal oils are also important BAS containing in the *B. tripartita* herb. n-Cymene (16.6%), a caryophyllene oxide (6.0%), and a humulene epoxide II (5.3%) are dominating components of the oil containing in flower heads of *B. tripartita*. Alloocimene (38.3%), (Z)-β-ocimene (30.6%), and α-phellandrene (8.5%) are the main components of the fresh herb oil.4

α-Pinene (15.0%), β-bisabolene (9.3%), n-cymene (6.0%), hexanal (5.7%), linalool (4.6%), n-cymene-9-ol (3.4%), β-element (2.6%), 2-pentylfuran (2.2%), and silfiperfol-6-en (2.1%) are the main components of the oil containing in the *B. tripartita* herb gathered in Bialystok (Poland) in August.[12]

Such groups of chemical compounds as monoterpene hydrocarbons, α-pinene (15.0%), n-cymene (6.0), sesquiterpene hydrocarbons, β-bisabolene (9.3%), belemen (2.6%), silfiperfol-6-en (2.1%), oxygenated monoterpenes, linalool (4.6%), n-cymene-9-ol (3.4%), aliphatic compounds, hexanal (5.7%), furan derivatives, and 2-pentylfuran (2.2%) are the main compounds containing in the oil.[12]

Various chemical compositions of ethereal oils extracted from various plants may be a reason for their various biological activity. Dominating plant components usually cause biological activity. α-pinene is the main compound of monoterpene hydrocarbons, which is dominating group of compounds containing in *B. tripartita*. According to data of some research, α-pinene is of good bacteriostatic and fungistatic properties though according to data of other research, the level of antimicrobic activity of α-pinene is low.[12]

Table 2: Biologically active compounds of the *B.* tripartita herb

Group of compounds	Name of compounds	Literary source in Tomczykowa M., 2011 format
Flavonoids	**Flavonols:** rutin, quercetin, axillarin, 3,6,30-trimethyl quercetagetin ether **Aurons:** sulfuretin, 6,7,30,40-tetrahydroxyauron **Flavanones:** 7-O-izookanin-glucoside, naringenin-7-glucoside **Catechins:**epicatechin, (+ -) – catechin, catechin hydrate, epigallocatechin gallate **Chalcones:** 3.20.40-threehydroxy-4-methoxychalcone, 40-O-b-D-glucopyranosyl-20.3-dihydroxy-4-methoxychalcone; butein, okanin, okanin 40-O-b-D-glucopyranoside, okanin 40-O- (600-O-acetyl-b-D-glucopyranoside), bidenoside G **Flavones:** flavone, diosmetin (O-methylated flavone). Phenylpropanoids: luteoside	Wolniak M., 2007 Tomczykowa M., 2008 Orhan N., 2016 Uysal S., 2018 Pozharitskaya O. N., 2010 Lv J. L., Zhang L. B., 2013 Korozhan T.V., Buzuk G. N., 2013
Aromatic hydroxy aldehydes	4-hydroxybenzaldehyde	Uysal S., 2018
Tannins	Tannin, catechin hydrate, and phenolcarboxylic acids	Uysal S., 2018 Pozharitskaya O. N., 2010
Polyacetylenes	2-b-D-glycopyrasyloxy-1-hydroxytrideka-3,5,7,9,11-pentain; 3 (R), 8 (E) -8-decene-4,6-diin-3, 10-dihydroxy-1-O-b-D-glucopyranoside.	Lv J. L., Zhang L. B., 2013
Phenolcarboxylic acids	Gallic acid, ellagic acid, linoleic acid, chlorogenic acid, caffeic acid, chicor acid, rosmarinic acid, neochlorogenic acid, n-hydroxybenzoic acid, gentisic acid, vanilic acid, 4-O-Caffeoylquinic acid, syringic acid, coumaric acid, ferulic acid, salicylic acid.	Tomczykowa M., 2008 Orhan N., 2016 Pozharitskaya O. N., 2010 Uysal S., 2018
Ethereal oil components	**Acyclic monoterpenes:** linalool, alloocimene, (Z)-β-ocimene **Monocyclic monoterpenes:** n-Cymene, α-phellandrene **Bicyclic monoterpenes:** α-pinene **Sesquiterpene:** β -bisabolene, β-elemen, silfiperfol-6-en, caryophyllene oxide, humulene epoxide II **Aromatic compounds:** n-cymene-9-ol **Aliphatic compounds:** hexanal **Furan derivatives:** 2-pentylfuran	Tomczykowa M., 2011 Tomczykowa M., 2008
Polysaccharides	neutral polysaccharides, sour polysaccharides, pectin	Pozharitskaya O. N., 2010
Coumarins	Umbelliferone, scopoletin, 6.7-dihydroxycoumarin	Pozharitskaya O. N., 2010

		Tomczykowa M., 2008 Tomczykowa M., 2011 Wolniak M., 2007 Orhan N., 2016 Serbin A. G., 1972
Others	Carotenoids, lactones, amines, and minerals; Thiophene, kosmen trails, and eugenol; Amino acids (arginine equivalents), organic acids (ascorbic acids, etc.); Volatile compounds: The B. tripartita petroleum extract consists of triterpenes, unsaturated aliphatic hydrocarbons, fatty acid and sterol ethers mostly consisting of stigmasterol.	Tomczykowa M., 2008 Tomczykowa M., 2011 Wolniak M., 2007 Pozharitskaya O. N., 2010 Orhan N., 2016

Pharmacological action :

Basing the results, the researched extracts are of antimicrobic activity. They are aqueous extract, aqueous methanol extract (1:1), aqueous acetone extract (1:1), and methanol extract (besides butanol extracts). However, they are not of fungistatic activity. Bacteriostatic action ethereal oils is low, but their antimycotic action is high. The results confirm, that it is possible to use *B. tripartita* to treat microbic infections. *B. tripartita* may be in use as antimicrobial drug, antimycotic drug, medicinal, or preserving agent.4

Ethereal oil is also of high antimycotic activity and low bacteriostatic effect. The *B. tripartita* aqueous extracts is of antiinflammatory action against severe rat pad swelling caused by carrageenan.[12]Antibacterial and antimycotic ethereal oil properties are estimated against eight gram-positive bacteria, 11 gram-negative bacteria, and 10 fungus strains. The oil is also of high antimycotic activity.[12]

Antimicrobic action :

Subextract of the *B. tripartita* herb ethereal extract is of the highest antimicrobic activity against gram-positive bacteria.4

Ethereal oils are of antimicrobic activity against gram-positive bacteria. Activity of flower oil is four times higher than ethereal herbal oil and a bit reduced growth of the both *E. coli* (gram-negative bacteria) strains. Action of the both ethereal oil might be recognized as unactive against *Klebsiella pneumoniae* and *Pseudomonas aeruginosa*.[4] Antimicrobic activity of 12 *B. tripartita* ethereal flower and herbal oil extracts is analyzed.[12]

B. tripartita ethereal root oil acts to reduce growth of gram-positive bacteria temperately in this research.[12]

Antimycotic action :

The ethereal oils are of high fungistatic effect, the highest one is against *Candida albicans* and *Candida parapsilosis*; the lowest one is against *Aspergillus fumigatus*.4

High antimycotic activity ethereal oils is also of a great importance. The oils might be recognized as possible alternative drugs to synthetic fungicides acting against plant pathogenic fungi.4 Thiophenes are one of the main oil components. It is possible that they also are of antimycotic activity.4,[24]

B. tripartita ethereal oil is of fungistatic effect. It is noted that *C. albicans* oil ATCC 10231 (MIC = 3.1 mg / ml) is of the most expressed inhibiting effect; *C. krusei* oil (MIC = 100 mg / ml) is of the lowest effect.[12] Ethereal oil extracted from *B. tripartita* roots is of high fungistatic activity, so it is possible to use it as a drug to treat plant pathogenic fungus.[12]

Antitumor and antithrombotic action :

The *B. tripartita* methylene chloride extract is of high antitumor activity against cancer cells L1210 (mouse leukemia) as well as antithrombotic activity.4,[25] The *B. tripartita* methylene chloride extract containing in the *B. tripartita* samples gathered in Krasnodar, in Khabarovsk, and in Perm (Russia) is of high antitumor activity against cancer cells L1210 (mouse leukemia) as well as antithrombotic activity.1,[25]

Cytotoxic action :

Viability of the MTT of three various cancer cell lines including cervical carcinoma HeLa, liver cancer Huh7, and breast cancer MDA-MB-231 are analyzed to study cytotoxic action of *B. tripartita*.[20] Large amount of luteolin-7-glucoside, containing in ethyl acelate and methanol extract, induces apoptotic causing accumulation of ROS and reduces β-catenin expression in the COLO 320 DM cells. Luteolin-7-glucoside may be in use as a strong antitumor drug to treat rectal cancer.[26] Dose-dependent antiproliferative effect of luteolin-7-glucoside is discovered at effect to human hepatocellular carcinoma HepG2 cells, the effect corresponds to the results of effect of ethyl acelate and methanol extracts to Huh7 cells.[20,27]

Antioxidant action :

Aqueous, aqueous-methanol, and aqueous-acetone *B. tripartita* extracts are potential sources of natural antioxidants, which may be in use in pharmaceutical and food industry.[13]

B. tripartita flowers and herb are antioxidant sources capturing radicals. Despite general contents of ethyl acelate, diethyl ethereal, and butanol herbal extracts include more phenols, radical capturing activity of flower extracts are higher than that of herbal extracts. That confirms that contents of general polyphenols, composition of extracts, and other factors (solvent and antioxidant synergism) are of a great importance to forecast antioxidant activity.[13] Chloroform subextract is of the highest antioxidant activity.[14] Aqueous, aqueous-methanol, and aqueous-acetone extracts of the *B. tripartita* above-ground parts are extracted with solvents. The extracts are of antiradical activity for the DPPH radicals. Analysis of antioxidant activity showed, that antiradical activity significantly related to flavonoids.1,[13]

Various experiments, including capturing free radicals (DPPH and ABTS), reducing power (CUPRAC and FRAP), and a capacity to bind phosphorus molybdenum and metals into chelate complexes are in use to estimate antioxidant activity of *B. tripartita*. The trolox equivalents (tuberculin unit/g of extract) show results of the experiments. A capacity to bind phosphorus molybdenum and metals into chelate complexes is estimated concerning EDTA (mg/g of extract). All antioxidant activity experiments are described above.[20,28]

In the research, various methods of antioxidant activity analysis are in use because various mechanisms of action might mediate antioxidant properties of the plant extracts. In the research, the following methods are in use to analyze antioxidant properties of the *B. tripartita* extract: analysis of capturing free radicals (ABTS and DPPH), analysis of reducing power (FRAP and CUPRAC), and the capacity to bind phosphorus molybdenum and metals into chelate complexes. The results are shown in table 3. Methanol extract (504.87 mgTE/g for DPPH and 460.59 mgTE/g for ABTS) are of the highest activity when capturing radicals.[20] Our results are equal to the results of the last researches[29,30,31] and confirm that usually, methanol extract is of the highest activity when capturing radicals in comparison with other extracts. Its the highest radical capturing activity may be explained by general contents of phenols.[20]

Methanol extract contains the highest general amount of phenols and flavonoids, it is of the highest reducing power (449.93 mgTE/g for CUPRAC and 299.21 mgTE/g for FRAP), the next is ethyl acelate (298.30 mgTE/g for CUPRAC and 201.77 mgTE/g for FRAP), and aqueous (242.73 mgTE / g for CUPRAC and 193.44 mgTE / G for FRAP) extracts.[20]

According to other antioxidant activity researches, ethyl acetate extract is of high general antioxidant activity and high capacity to bind metals into chelate complexes.[20]

Antioxidant properties of *B. tripartita* may be caused by its phenol components (including chlorogenic acid, epicatechin, and luteolin-7-glucoside).[20]

Antidiabetic action and enzyme inhibiting effect :

B. tripartita is of high antidiabetic action. Its active components may be in use to treat diabetes and diabetes complications.[14] Chloroform, ethyl acelate, n-butanol, and permanent *B. tripartita* aqueous extract significantly decreases glucose level of blood (11.5-25.8%) of the rats suffering from normoglycemia and of the rats suffering from glucose loading in comparison with healthy dose-dependent controlled group. Besides, it is discovered that the *B. tripartita* ethanol extract is of antidiabetic activity and it is a strong drug (14.0-32.7%) to treat the rats suffering from diabetes, caused by Streptozotocin.[14]Antidiabetic effect of ethyl acelate and n-butanol extract is higher than, that of other subextracts. The results of our experiments show that ethanol extract is of high hypoglycemic action on the rats suffering from normoglycemia and the rats suffering from glucose loading. There is an opportunity that it is also of antidiabetic action on the rats suffering from diabetes, caused by acute or subacute introduction of Streptozotocin. Chloroform, ethyl acelate, n-butanol, permanent aqueous extract, and ethanol extract of *B. tripartita*, which contain chlorogenic acid, cynaroside, and luteolin, are of antidiabetic activity, despite various mechanisms of action.[14]

According to the description made by Orhan et al. (2016)[14], extracts of ethyl acelate and n-butanol *B. tripartita* extracts are of high antidiabetic activity upon the in vivo analysis. They also note, that extract of ethyl acelate extract is of strong inhibitting effect on α-amylase (22.12% by 2 mg / ml) and on α-glycosidase (64.56% by 2 mg / ml).[20]

The results, got by Orhan et al. (2016)[14] and Oboh et al. (2015)[32], show, that there is a relationship between phenol components (including chlorogenic acid, luteolin, and luteolin-7-glucoside) and antidiabetic activity.[20]

Enzyme inhibiting activity :

There is a literature data on inhibiting action of *B. tripartita* on the following enzymes: acetylcholinesterase (ACHE), butyrylcholinesterase (BCHE), α-amylase, and α-glycosidase.[20,33,34,35,36,37]

Enzyme inhibiting effect :

Ethyl acelate extract is of the highest inhibiting activity relating to α-amylase (1.22 mmolACAE/g), while methanol extract is of the highest inhibiting effect relating to α-glycosidase (22.22 mmolACAE/g).[20]

Antiinflammatory + analgesic + antipyretic action :

The *B. tripartita* infusions reduced rat pad inflammation caused by carrageenan during 3 hours. In the research, we noted analgesic effect of the infusion. Antipyretic effect of aqueous infusions is significant shorter for dose of 20 ml by kg in comparison with 5 mg of indomethacin by kg of weight.1

We can suggest that antiinflammatory activity of the *B. tripartita* infusions is caused by synergic action of polyphenols, polyacetylenes, coumarins, triterpenes, and other active compounds.1 Table 4 shows antipyretic effect of *B. tripartita* infusion.1

DNA protection :

B. tripartita protective effect on supercoiled plasmid pUC19 DNA is analyzed earlier.[20,38]

DNA protection effects :

All the *B. tripartita* extracts protect supercoiled form of plasma pUC19 (> 70%). It is discovered that aqueous extract (10 mg / ml) and ethyl acelate extract (10 mg/ml) are of the most effective protection effect (80%). Based on the HPLC analysis, chlorogenic acid and luteolin-7-glucoside are the most prevailing phenol compounds discovered in the *B. tripartita* extracts. The documents confirmed, that chlorogenic acid is of antioxidant and antimutagenic activity in vitro.[39] Radical capturing activity of luteolin-7-glucoside is also analysed relating to the DPPH radical. It is recognized that clean form of the DPPH radical captures radicals effectively.[13] Consequently, this research confirms that high level of chlorogenic acid and of luteolin-7-glucoside containing the *B. tripartita* extracts causes the DNA protection effects.[20]

Other pharmacological effects :

The *B. tripartita* herb is in use as a diuretic, hiidrotic, antiinflammatory, and immunostimulating drug in folk medicine. The *B. tripartita* herb is also an effective drug to treat blood vessel damages and any bleedings. It may be in use to treat cutaneous diseases, fever, urolithiasis, calculus, bladder, and kidney diseases.4[,40,] The *B. tripartita* herb is usually in use to treat a range of such diseases as urolithiasis and other kidney and bladder diseases. *B. tripartita* is in use in folk medicine to treat fever and various bleedings. It is an effective antiinflammatory drug. *B. tripartita* is of immunostimulating action. It is also in use to treat cutaneous diseases and vessel damages. It is discovered that methylene chloride containing in the *B. tripartita* extract is of high inhibitory activity against cancer cells L1210 (mouse leukemia) as well as antithrombotic activity.[12] The *B. tripartita* herb is in use as a diuretic, hiidrotic, and antiinflammatory drug in folk medicine. It is also in use to treat fever, cutaneous diseases, bladder diseases, kidney diseases, and as a immunostimulating drug.[13]

It is noted above, that *B. tripartita* is an effective drug to treat children allergic itch. Methylene chloride containing in the *B. tripartita* extract is of high antitumor activity for the L1210 cancer (mouse leukemia) and antithrombotic activity.[13] The *B. tripartita* above-ground part infusion is in use to treat catarrhal rhinitis, angina, acute respiratory infections, and as an antiinflammatory drug against colitis, gout, and childhood rickets in Russian folk medicine. It is also in use as a hiidrotic drug and as a diuretic drug to treat urolithiasis and as an antiseptic and antiallergic drug to make baths for children. Decoctions made from various kinds of *B. tripartita* is in use to treat sugar diabetes.[14,42,43,44]

There are multiple pharmacological studies on *B. tripartita* herb and, according to the literature data, it is of antitumor, antiinflammatory, antimicrobial, antioxidant, antithrombotic, antiulcerogenic, hepatoprotective, and hypotensive effect.[14] Antiinflammatory activity, analgetic, and antipyretic properties are discovered.1

The *B. tripartita* infusions are widely in use in native folk medicine to treat catarrhal rhinitis, angina, ARD, as well as an antiinflammatory drug to treat colitis, gout, and rickets.[43] The *B. tripartita* infusions are in use in Chinese folk medicine to treat chronic dysentery.[45] The infusion is also in use as a hiidrotic and diuretic drug to treat urolithiasis, to make childhood baths, mainly against diathesis (antiallergic action) in East medicine.1[,44]

The *B. tripartita* infusion is generally in use in folk medicine to treat cold and infection illnesses, and it is in use perorally. Aqueous extract is of antiinflammatory, analgesic, antipyretic properties for rats.1 Antiproliferative, antioxidant, and antitumor properties, as well as DNA protection, are characteristic properties of the *B. tripartita* herb.[20]

Basing on the last researches, various kinds of *B. tripartita* are of biological activity, including antioxidant, antidiabetic, antitumor, and antiinflammatory activity.[14,46] These effects are may be in use by phenol components (mainly flavonoids), which are included as compounds of their chloroform, ethyl acelate, n-butanol, permanent aqueous subextracts, and ethanol extracts.[20]

It is discovered that *B. tripartita* is of antioxidant activity, DNA protection activity, inhibition activity for the main enzymes, which participate in such widespread patologies as diabetes and neurodegenerative diseases in vitro. It is also established that *B. tripartita* is of antiproliferative action, which may be in use to treat cancer later. The biological properties may be in use by presence of bioactive secondary metabolites, from which such chemical compounds, as chlorogenic acid, epicatechin, and luteolin-7-glucoside are registered. They are the main phenol components of the *B. tripartita* extracts.[20]

General composition of various parts of *B. tripartita* plant:

1) Flowers and herb: izookanin-7-O-glucoside, luteolin-7-O-glucoside (cynaroside), and luteolin → antioxidant action[13];

2) Above-ground parts:

1. Chlorogenic Acid, luteolin, and cynaroside[14]
2. Butein, luteolin, okanin, 3.2'4'-threehydroxy-4-methoxychalcone diosmetin2 → antioxidant, antidiabetic effect;

3) Above-ground parts: chlorogenic acid, (±)-catechin, rosmarinic acid, luteolin-7-O-glucoside → antiinflammatory effect.1,[20]

It is officially established that the *B. tripartita* herb medicinal plant raw material extracted from *B. tripartita*, is of antioxidant, antimicrobial, antimycotic, hepatoprotective, immunostimulating, and hypotensive activity. The activities may be in use by flavonoids (flavones, chalcones, and aurons), ethereal oil, and polyacetylenes containing in the *B. tripartita* herb compounds.[23]

MATERIALS AND METHODS:

There is a content analysis of various data sources. They are electronic search systems (Google and Google academy), scientific literature, and electronic data bases (e-Library, Pubmed, Cyberleninka, Scopus, and Web of Science).

CONCLUSION:

The analysis showed that *B. tripartita* is of multiple pharmacological effects. Antimycotic, antiinflammatory, antimicrobial, hypotensive, antioxidant, immunostimulating, antithrombotic, antiradical, antidiabetic, antiulcerogenic, antitumor, analgesic, antipyretic, antiallergic, hepatoprotective activities of *B. tripartita,* inhibition activity for the main enzyme, and DNA protection activity are caused by presence of flavonoids (luteolin glycosides, aurons, chalcones, flavones, etc,), ethereal oil, phenolcarboxylic acid, polysaccharides, aromatic hydroxy aldehyde, coumarins, tannins, polyacetylenes, and other important BASes in the *B. tripartita* herb.

Nowadays, *B. tripartita* is commonly in use as diuretic, hiidrotic, antiinflammatory, and immunostimulating drug to treat blood vessel damages, any bleedings, cutaneous diseases, fever, urolithiasis, calculus, bladder diseases, kidney diseases, and childhood allergic itch in folk medicine. The *B. tripartita* herb infusions are widely in use in native folk medicine to treat catarrhal rhinitis, angina, acute respiratory infections, as well as an antiinflammatory drug to treat colitis, gout, and childhood rickets. It is also in use to treat chronic dysentery and as an antiallergic and antiseptic drug to make baths for children.

The *B. tripartita* medicinal plant raw material may be in use to make potential antibacterial, antimycotic, and antitumor drugs. It should be noticed that additional pharmacogenetic and pharmacological researches are necessary to give additional information to wide field of use of this medicinal plant in official medicine. The methods of standardization of a plant raw drug should also be developed.

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CONFLICTS OF INTEREST:

None.

REFERENCES:

1. Pozharitskaya ON, Shikov AN, Makarova MN, Kosman VM, Faustova NM, Faustova NM, et al. Anti-inflammatory activity of a HPLC-fingerprinted aqueous infusion of aerial part of Bidens tripartita L. Phytomedicine : international journal of phytotherapy and phytopharmacology. 2010; 17(6): 463-468.
2. Lv J-L, Zhang L-B. Flavonoids and polyacetylenes from the aerial parts of Bidens tripartita. Biochemical Systematics and Ecology. 2013; 48: 42-44.
3. Plantarium URL: https://www.plantarium.ru/page/image/id/681135.html
4. Tomczykowa M, Tomczyk M, Jakoniuk P, Tryniszewska E. Antimicrobial and antifungal activities of the extracts and essential oils of Bidens tripartita. Folia Histochemica et Cytobiologica. 2008; 46(3): 389-393.
5. Barańska K. Studies on some flavonoids present in herbs of Bidens tripartitus L. Acta Polon Pharm. 1963; 20: 357-364.
6. Serbin AG, Borisov MJ, Chernobai VT, Kovalev IP, Gordienko VG. Flavonoids of Bidens tripartita. III. Khim Prirod Soedin. 1975; 11: 144-147.
7. Isakova TI, Serbin AG, Belikov VV, Chushenko VN. Flavonoids and polysaccharides of Bidens L. species. Rastit Resur. 1986; 22: 517-523.
8. Olejniczak S, Ganicz K, Tomczykowa M, Gudej J, Potrzebowski J. Structural studies of 2-(3',4'-dihydroxyphenyl)-7- - D-glucopyranos-1-O-yl-8-hydroxy-hroman-4-one in the liquid and solid states by means of 2D NMR spectroscopy and DFT calculations. J Chem Soc, Perkin Transactions 2. 2002; 6: 1059-1065.
9. Serbin AG, Zhukov GA, Borisov MJ. Coumarines from Bidens tripartita. Chemistry of Natural Compounds. 1972; 8(5): 652.
10. Tomczykowa M, Gudej J, Majda T, Góra J. Essential oils of Bidens tripartita L. J Essent Oil Res. 2005; 17: 632-635.
11. Ben'ko GN. Effect of gamma-irradiation of Bidens tripartite L. seeds on plant yields and accumulation of biologically active compounds. Rastit Resur. 1983; 19: 516-520.
12. Tomczykowa M, Leszczyńska K, Tomczyk M, Tryniszewska E, Kalemba D. Composition of the essential oil of Bidens tripartita L. roots and its antibacterial and antifungal activities. Journal of medicinal food. 2011; 14(4): 428-433.
13. Wolniak M, Tomczykowa M, Tomczyk M, Gudej J, Wawer I. Antioxidant activity of extracts and flavonoids from Bidens tripartita. Acta poloniae pharmaceutica. 2007; 64(5): 441-447.

14. Orhan N, İçöz ÜG, Altun L, Aslan M. Anti-hyperglycaemic and antioxidant effects of Bidens tripartita and quantitative analysis on its active principles. Iranian journal of basic medical sciences. 2016; 19(10): 1114-1124.
15. Christensen LP, Lam J, Thomasen, T. A chalcones and other constituents of Bidens tripartitus. Phytochem. 1990; 29: 3155-3156.
16. Mikayelyan AS, Oganesyan ET, Stepanova EF, Krikova AV. Bur-marigold (Bidens tripartita L.) polyphenols: composition and biological properties. FARMATSIIA-MOSKVA-. 2008; 1: 33.
17. Mojab F, Kamalinejad M, Ghaderi N, Vahidipour HR. Phytochemical screening of some species of Iranian plants. Iranian Journal of Pharmaceutical Research. 2003; (2): 77–82.
18. Olennikov DN, Tankhaeva LM. Technique of quantitative definition of group structure of the carbohydrate complex of plant objects. Khimiya Rastitel'nogo Syr'ya. 2006; 10: 29–33.
19. Williams DJ, Edwards D, Hamernig I, Jian L, James AP, Johnson SK, et al. Vegetables containing phytochemicals with potential anti-obesity properties: A review. Food Research International. 2013; 52(1): 323-333.
20. Uysal S, Ugurlu A, Zengin G, Baloglu MC, Altunoglu YC, Mollica A, et al. Novel in vitro and in silico insights of the multi-biological activities and chemical composition of Bidens tripartita L. Food and chemical toxicology : an international journal published for the British Industrial Biological Research Association. 2018; 111: 525-536.
21. Sagdic O, Ozturk I, Ozkan G, Yetim H, Ekici L, Yilmaz MT. RP-HPLC–DAD analysis of phenolic compounds in pomace extracts from five grape cultivars: Evaluation of their antioxidant, antiradical and antifungal activities in orange and apple juices. Food Chemistry. 2011; 126(4): 1749-1758.
22. Wojdyło A, Oszmiański J, Czemerys R. Antioxidant activity and phenolic compounds in 32 selected herbs. Food Chemistry. 2007; 105(3): 940-949.
23. Korozhan NV, Buzuk GN. THE COMPARATIVE ANALYSIS OF COMPONENT COMPOSITION OF BIDENS SPECIES BY LC. Bulletin of Pharmacy. 2013; 4: 49-56.
24. Mares D, Tosi B, Poli F, Andreotti E, Romagnoli C. Antifungal activity of Tagetes patula extracts on some phytopathogenic fungi: ultrastructural evidence on Pythium ultimum. Microb Res. 2004; 159: 295-304.
25. Goun EA, Petrichenko VM, Solodnikov SU, Suhinina TV, Kline MA, Cunningham G, et al. Anticancer and antithrombin activity of Russian plants. Journal of Ethnopharmacology. 2002; 81(3): 337-342.
26. Baskar AA, Ignacimuthu S, Michael GP, Al Numair KS. Cancer chemopreventive potential of luteolin-7-O-glucoside isolated from Ophiorrhiza mungos Linn. Nutrition and cancer. 2011; 63(1): 130-138.
27. Hwang YJ, Lee EJ, Kim HR, Hwang KA. Molecular mechanisms of luteolin-7-O-glucoside-induced growth inhibition on human liver cancer cells: G2/M cell cycle arrest and caspase-independent apoptotic signaling pathways. BMB reports. 2013; 46(12): 611.
28. Zengin G, Uysal S, Ceylan R, Aktumsek A. Phenolic constituent, antioxidative and tyrosinase inhibitory activity of Ornithogalum narbonense L. from Turkey: a phytochemical study. Industrial Crops and Products. 2015; 70: 1-6.
29. Pavithra K, Vadivukkarasi S. Evaluation of free radical scavenging activity of various extracts of leaves from Kedrostis foetidissima (Jacq.) Cogn. Food Science and Human Wellness. 2015; 4(1): 42-46.
30. Sowndhararajan K, Kang SC. Free radical scavenging activity from different extracts of leaves of Bauhinia vahlii Wight & Arn. Saudi journal of biological sciences. 2013; 20(4): 319-325.

31. Uysal S, Zengin G, Locatelli M, Bahadori MB, Mocan A, Bellagamba G, et al. Cytotoxic and enzyme inhibitory potential of two Potentilla species (P. speciosa L. and P. reptans Willd.) and their chemical composition. Frontiers in pharmacology. 2017; 8: 290.
32. Oboh G, Agunloye OM, Adefegha SA, Akinyemi AJ, Ademiluyi AO. Caffeic and chlorogenic acids inhibit key enzymes linked to type 2 diabetes (in vitro): a comparative study. Journal of basic and clinical physiology and pharmacology. 2015; 26(2): 165-170.
33. Mocan A, Zengin G, Simirgiotis M, Schafberg M, Mollica A, Vodnar DC, et al. Functional constituents of wild and cultivated Goji (L. barbarum L.) leaves: phytochemical characterization, biological profile, and computational studies. Journal of enzyme inhibition and medicinal chemistry. 2017; 32(1): 153-168.
34. Mocan A, Zengin G, Uysal A, Gunes E, Mollica A, Degirmenci NS, et al. Biological and chemical insights of Morina persica L.: A source of bioactive compounds with multifunctional properties. Journal of Functional Foods. 2016; 25: 94-109.
35. Zengin G. A study on in vitro enzyme inhibitory properties of Asphodeline anatolica: New sources of natural inhibitors for public health problems. Industrial Crops and Products. 2016; 83: 39-43.
36. Kim J-S, Kwon C-S, Son KH. Inhibition of alpha-glucosidase and amylase by luteolin, a flavonoid. Biosci Biotechnol Biochem. 2000; 64: 2458-2461.
37. Tadera K, Minami Y, Takamatsu K, Matsuoka T. Inhibition of α-glucosidase and α-amylase by flavonoids. J Nutr Sci Vitaminol. 2006; 52: 149-153.
38. Yerlikaya S, Zengin G, Mollica A, Baloglu MC, Altunoglu YC, Aktumsek A. A multidirectional perspective for novel functional products: in vitro pharmacological activities and in silico studies on Ononis natrix subsp. hispanica. Frontiers in pharmacology. 2017; 8: 600.
39. Rice-Evans CA, Miller NJ, Paganga G. Structure-antioxidant activity relationships of flavonoids and phenolic acids. Free radical biology and medicine. 1996; 20(7): 933-956.
40. Ozarowski A. Lexicon of natural drugs. Agencja Wydawnicza COMES, Katowice, Poland. 1993; 205.
41. Strzelecka H, Kowalski J. Encyclopaedia of herbal medicines and phytotherapy. PWNPress, Warszawa. 2000; 327.
42. Blinova KF, Yakovlev GP. Botanical Pharmacognostic Dictionary. Moscow: Vysshayashkola. 1990.
43. Sokolov SY. Phytotherapy and Phytopharmacology: The manual for doctors. Moscow: Medical News Agency. 2000; 197-199.
44. Sezik E, Yesilada E, Shadidoyatov H, Kulivey Z, Nigmatullaev AM, Aripov HN, et al. Folk medicine in Uzbekistan I. Toshkent, Djizzax, and Samarqand provinces. J Ethnopharmacol. 2004; 92: 197-207.
45. Zhang S. Treatment of 500 cases of dysentery with Bidens tripartita. Shandong Journal of Traditional Chinese Medicine. 1989; 8: 11–12.
46. Bartolome AP, Villaseñor IM, Yang WC. Bidens pilosa L.(Asteraceae): botanical properties, traditional uses, phytochemistry, and pharmacology. Evidence-based complementary and alternative medicine. 2013.