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Comparative flavonoids content of *Taraxacumofficinale* vegetal organs extracts from different Romanian regions

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ABSTRACT

An important scientific interest has been given to the potential health-promoting properties of flavonoids due to their discovered wide range of activities in the prevention of common diseases, including coronary heart disease, cancer and other disorders. These effects came out to be related to the various biological or pharmacological activities of flavonoids, including antimicrobial, immunomodulatory or antithrombotic activities. Plants of the Taraxacum genus are being used as an herbal remedy to prevent, manage, and even ameliorate such human disorders due to its wide range of phytochemicals. The present paper emphasises the comparative content of flavonoids from vegetal organs of Taraxacum officinale F.H. Wigg (dandelion), perennial plant collected from different regions of Romania and evaluates the antioxidant potential of dandelion hydroalcoholic extracts. Mature vegetal product was collected in May 2022, from the eastern area of Transylvania, southern area of Dobrogea and Central Plateau of Moldova. The fresh plant was dried, ground to a fine powder and extracted 10% concentration, in 50:50 (v:v) ethanol and 70:30 (v:v) ethanol, using the conventional method of cold maceration. The obtained hydroalcoholic extracts were analysed by UV-Vis spectrophotometry. Total flavonoids concentration was highest in ethanol extracts of the plants collected from the Moldova region for all analysed vegetal organs - Radix, Herba, Flower and Mix. The influence of climate and soil on Taraxacum officinale plants from Dobrogea, *Moldova and Transylvania areas determined significantly different values of the concentration of bioactive principle analysed and supports us to continuate the studies on the content of bioactive principles and the therapeutic activity of this valuable vegetal product from the Romanian spontaneous flora.*

Keywords: *Taraxacum officinale, dandelion, flavonoids, hydroalcoholic extracts, vegetal organs*

INTRODUCTION

Flavonoids are a wide class of plant secondary metabolites belonging to the larger family of natural polyphenols. They are often present in fruits, vegetables, nuts, plant-derived beverages such as tea and wine, and in some traditional herbal medicines, thus covering an important part of the human diet. More than 6000 naturally flavonoids have been described in different plants; these flavonoids show many healthful effects with a lot of advantages over chemical treatments. Plant flavonoids were originally considered important in plant pigmentation and flavour [Ross et al, 2002]; later on, they were accredited to play a significant role in plant growth and reproduction, also providing resistance to pathogens and predators and so, protecting crops from diseases [Bravo, 1998]. They can also function as stress protectors in plant cells by scavenging the reactive oxygen species (ROS) produced by the photosynthetic electron transport system and by UV radiation [Shirley, 1996]. The ability of flavonoids to balance ROS as well as phytohormone signalling may help to explain their involvement in stress-induced morphogenic responses, a general response of plants to 'fly away' from pernicious environmental conditions. For example, valuable antioxidant flavonoids, dispersed in the chloroplast, the nucleus and the vacuole of mesophyll cells, represents more than 90% of the total flavonoid stock in plants inhabiting stark, sunny habitats, and display dense phenotypes, with little and thick leaves and tiny internodes [Brunetti et al, 2018]. For a long time, flavonoids were considered as primarily synthesised to represent an successful shield against the penetration of UV-B radiation to sensitive leaf tissues, and greatly involved in protecting plants challenged by the diminution of stratospheric ozone layer [Bais et al., 2018]. Flavonoids play different roles in the ecology of plants: flavones, flavonols and anthocyanidins, through their attractive colours, may act as visual signals for pollinating insects, whereas flavanols, thanks to their astringency, are a defence system against insects [Bravo, 1998]. In the 2022 study on the dandelion from the Dobrogea area, collected in autumn (September-October, 2021), in cold macerated hydroalcoholic extracts it was found the highest total flavonoids content of 36.514±140.3 mg/kg DW for leaves extract (coded Herba) in ethanol 70%, compared to root extract 28.167±138.5mg//kg DW and the whole plant extract - 19.782±140.5 mg/kg DW *Taraxacum* also in 70:30 (v:v) ethanol. The Soxhlet extraction of the bioactive principles from *Taraxacum* organs revealed in hydroalcoholic extracts a total flavonoids value of 8.96 g/kg DW in Herba and 18.86 g/kg DW in Radix (Tănasă et al., 2022a). Previous studies of hydroalcoholic extracts from plant organs - root, leaves and the whole plant of *Taraxacum officinale* F.H. Wigg (dandelion),emphasised a better extraction of some bioactive substances e.g., tannins, beta-carotene and lycopenpigments in 70:30 (v:v) ethanol, respectively, anthocyanins in 50:50 (v:v) ethanol (Tănasă et al., 2022b).

Flavonoids structure and subclasses

Flavonoids are named from the Latin word "*flavus*", meaning *yellow*; they are secondary metabolites of plants and fungi and have a 15-carbon skeleton containing two phenyl rings and a heterocyclic ring. [Roman-Blass and Jimenez, 2006; Newman and Cragg, 2007]. So, they have a basic chemical structure of diphenyl propanes, consisting of two benzene rings joined by a linear three-carbon chain (C6-C3-C6). In most cases, the central three carbons form a closed pyran ring with one of the benzene rings, thus forming a structure of 15 carbon atoms arranged in three rings, labelled A, B and C. The different classes of flavonoids varies in the degree of oxidation and in the arrangement of substitution of the C ring, while individual compounds within a class differ in the pattern of substitution of the A and B rings [Hertog et al., 1993]. The chemical variety of flavonoids is developed on two structural differences; namely the arrangement of substitution of the C ring that depends on the carbon on which the B ring is attached, and the degree of oxidation of the C ring [Panche et al., 2016; Brodowska, 2017]. The basic flavonoid structure is aglycone, but they typically occur in nature as glycoside and methylated derivatives, which are products of secondary metabolism in plants [Kumar and Pandey, 2013].

Depending on the variations in the heterocyclic C-ring, flavonoids may be divided into seven subclasses: flavones (e.g., apigenin, luteolin, diosmetin, chrysin), flavonols (quercetin, kaempferol, myricetin, galangin, fisetin), flavanones (e.g., naringenin, hesperitin, erioclictyol), flavanonols (taxifolin), flavanols or catechins (catechin, epicatechin, epigallocatechin, epigallocatechin gallate), isoflavones (genistein, daidzein, glycitein, puerarin), anthocyanins and anthocyanidins (cyanidin, pelargonidin, delphinidin, malvadin, petunidin).

In almost all subclasses, ring B is linked at C2 with ring C, with only one exception - of the isoflavones (linked at C3). Flavones, flavonols and isoflavones show a double bond between C2 and C3, whereas flavanones, flavanonols, and flavanols contain a saturated three-carbon chain. These subclasses differ among them by the presence of a carbonylic carbon atom at C4 (flavones, flavonols, flavanones, flavanonols, and isofla-vones) and a hydroxyl group at C3 (flavonols, flavanonols, and flavanols) [Manach et al., 2004]. The anthocyanins are glycosides, providing glucose, galactose, rhamnose, xylose or arabinose conjugated to the aglycon nucleus via the C3 hydroxyl group. The de-glycosylated or aglycone forms of the anthocyanins are known as anthocyanidins; these are salt derivatives of the 2-phenylchromenylium cation, also known as the flavylium cation [Manthey, 2005].

Some structural modifications might support the anti-inflammatory activities of the flavonoids. Current studies on the structural requirements demonstrates that the unsaturation of the C ring, the presence of a carbonyl group on C-4, the number and position of hydroxyl groups, and glycosylation status affect the anti-inflammatory properties of flavonoids [Lago et al., 2014]. Another example, the hydroxylation pattern of the B ring of certain flavonoids facilitate the inhibition of cytokine secretion by mast cells and macrophages [Kim et al., 2004]. Glycosylation of flavonoids has been closely related to a decrease in the inhibitory effect on inflammation because glycoside derivatives are more promptly absorbed than aglycones.

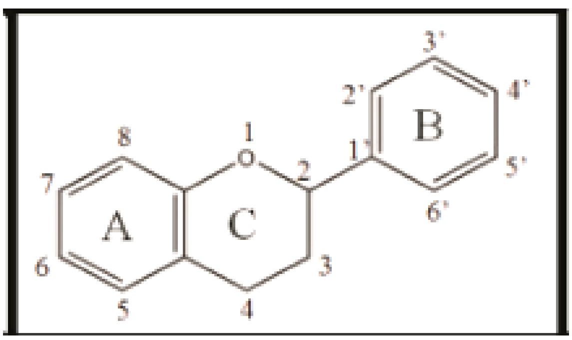

Fig. 1. Basic structure of a flavonoid
(adapted after Hossain et al., 2016)

A wide range of biological activities have been assigned to the flavonoid group of natural products. These include anti-oxidant, anti-inflammatory, anti-mutagenic, anti-viral, and anti-allergic properties. Due to their structure, flavonoids engage various protective effects against several chronic diseases like cancer, diabetes, and cardiovascular disorders, as well as neurodegenerative conditions. By complexing with oxidizing species, hydroxyl groups in flavonoids render these compounds the ability to scavenge and stabilize free radicals, reducing oxidative damage, which is the hallmark of several chronic diseases [Kumar and Pandey, 2013].

Flavonoids in Cancer - flavonoids have been demonstrated to inhibit tumor cell proliferation via inhibition of ROS formation, as well as suppression of xanthine oxidase, COX-2, and 5-LOX, which are the major catalysts for tumor promotion and progression [Chahar et al., 2011]. Other studies proved that cyclin dependent kinases (CDKs) are key regulators of cell cycle progression, immune cell activation, neoangiogenesis, and inflammation [Schmitz et al., 2016].

Flavonoids in Diabetes - inflammation has long been connected with the development of type 1 diabetes, however, some other studies have demonstrated that chronic low-grade inflammation might be responsible for onset and/or exacerbation of diabetes mellitus or type 2 diabetes. [Pollack et al., 2016] It has been revealed that flavonoids can adjust carbohydrate and lipid metabolism, diminish hyperglycemia, insulin resistance, reduce oxidative stress and stress-sensitive signaling pathways [Choi and Kim, 2009]. Flavonoids helped the organisms re-establish glucose homoeostasis attenuating the diabetic condition, but also restrict the secondary damage to the different peripheral organs. Chrysin prevents the development of diabetic neuropathy and increases cognition, improves renal pathology in diabetic rats [Ahad et al., 2014; Li et al., 2014] and hesperidin enhanced heart function in diabetic rats [Visnagri et al., 2014, Agrawal et al., 2014].

Flavonoids in Neuroinflammation - neuroinflammation is accompanying several neurodegenerative diseases such as Alzheimer’s disease, Parkinson’s disease, Huntington’s disease and multiple sclerosis. Activation of central nervous system resident microglial cells is one of the vital events in the inflammatory cascade, which leads to the advancement of neurodegeneration [Gonzalez and Pacheco, 2014]. These inflammatory incidents contribute to the apoptotic cell death of neurons in many neurodegenerative diseases.Natural flavonoids have been demonstrated to exert neuroprotective activities by inhibiting the release of pro-inflammatory cytokines; they also exert an anti-inflammatory effect by interfering with the development of inflammatory mediators such as IL-6, TNF-α, and IL-1β in several cell lines through the MAPK signaling pathway [Li et al., 2015]. Several epidemiological studies indicate that consumption of flavonoids such as quercetin and catechins is associated with a lower incidence of Parkinson’s disease [Checkoway et al, 2002] and Alzheimer’s disease (AD) [Scarmeas et al., 2006]. Of note, the ability of flavonoids to cross the blood-brain barrier (BBB) is favored by their relatively high lipophilicity [Youdim et al., 2003] and depends on the interaction with specific efflux transporters present in the BBB [Lin and Yamazaki, 2003].

Flavonoids in Cardiovascular Disorders - inflammatory mediators are a predictive and also a causative factor in the pathogenesis of cardiovascular disorders. Because of the phenol hydroxyl groups present in flavonoids, these compounds possess remarkable anti-oxidant and free-radical scavenging properties. Thus, these polyphenols are able to display promising effects in the management of cardiovascular injury. In vitro evidence shows that quercetin reduces LDL oxidation at physiological levels in human umbilical vein endothelial cells

[Kostyuk et al., 2011]. Similar decrease in macrophage-mediated LDL oxidation was experienced after treatment with fisetin and proanthocyanidins [Al-Awwadi et al., 2005].

Clinical studies on flavonoid-rich foods have not focused on disease endpoints, and most studies have used foods rather than purified flavonoids. These studies have shown that foods rich in dietary flavonoids such as cocoa, tea, purple grape juice, and soy have biological effects within the cardiovascular system. However, these findings are not sufficient to conclude that consumption of foods rich in dietary flavonoids will help reduce CVD risk [Erdman et al., 2005]. Although an extensive amount of information has been presented on flavonoids, the need for further research in this area is clearly evident. Therefore, determination of flavonoids from natural sources must be encouraged for accurate identifications.

The aim of this paper was to assess the comparative concentration of flavonoids from vegetal organs of dandelions collected from three different regions of Romania, to highlight the content of bioactive principles and the therapeutic activity of this valuable vegetal product from the Romanian spontaneous flora.

MATERIAL AND METHODS

Mature vegetal product of *Taraxacum officinale* was collected in May 2022, from the eastern area of Transylvania, Harghita county (46°31′16″N 25°39′24″E), from the southern area of Dobrogea, Constanța county (44°23′36″N 28°58′46″E) and from the Central Plateau of Moldova region, Romania (47°06′00″N 26°.74′44″E), in the northeastern part of Neamt County, Romania (north:48°15′N 26°43′E; south 43°40′N 25°22′E; west 46°08′N 20°19′E; est 45°09′N 29°40′E). Dobrogea has typical chernozemic and calcareous soils, with an average annual temperature of 11-13 °C because the climate is temperate-continental, close to subtropical-humid, with certain peculiarities related to the physical-geographical components of the territory of the Black Sea proximity, and the average temperature of May was 16-18 °C. The average of 2022 in terms of precipitation was between 200-400 mm. Harghita has average annual temperature of 4-6 °C and the average temperature of May was 12-14 °C because of the special climate; it is temperate-continental, with certain particularities determined by the alternation of the mountain massifs with the series of intramontane depressions and the approximately perpendicular orientation of the relief units to the atmospheric circulation of air masses, and the soils are a combination of acidic podzolic clay-alluvial soils, brown and podzolic clay-alluvial soils, lithomorphic soils. In 2022 the precipitation was between 700-800 mm on average per year. The Central Plateau of Moldavia is based, from a geomorphological point of view, on sands and gravels over which finer clay-sand deposits (loessoid clays) are placed and falls within a slightly moderate continental temperate climate characterised by average annual temperatures ranging from 8 and 9 °C and in May the average temperature was 13-15 °C, and precipitation between 550 and 600 mm on average per year.

The biological material was represented by roots (coded Radix, Fig. 2.A), whole plant (coded Mix, Fig. 2.B), scapes and leaves (coded Herba, Fig. 2.C) and flowers (Fig. 2.D), collected from plants at full maturity and all parts of the plant were separated, washed thoroughly with tap water. Fresh plant was dried at room temperature on metal sieves and grind to a fine powder.

Vegetal fluid extracts were obtained using the conventional method of cold maceration for 14 days at ambient temperature, followed by normal pressure filtration. For cold maceration, *Taraxacum* powders were mixed with 50:50 (v:v) and 70:30 (v:v) ethanol in a conical flask – 10 g/100 mL. The mixture was stirred thoroughly with a glass rod. The conical flask was kept with intermittent shaking for 14 days, in darkness. The mixture was filtered at normal pressure through quantitative Whatman filter paper; extractive solutions present various colours, from light-brown to green-brown (Fig.3).

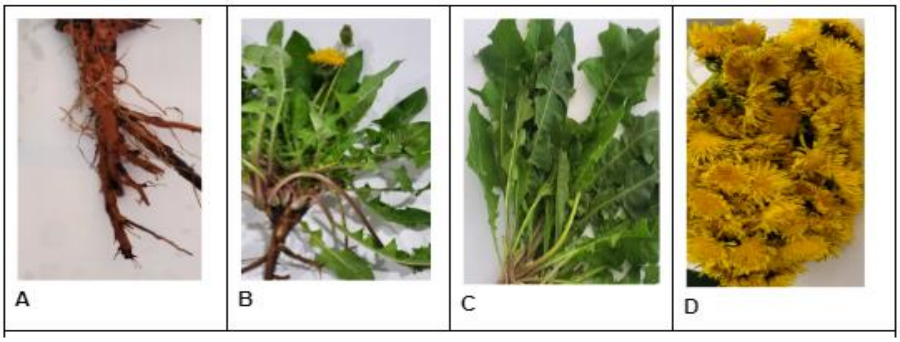

Fig. 2.*Taraxacum officinale* vegetal organs: (A) Radix; (B) Mix; (C) Herba; (D) Flower (original photos, Tănasă (Acreței) M.V.)

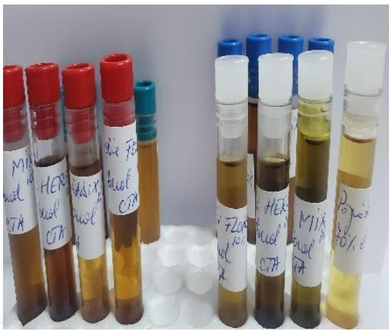

Fig. 3.Hydroalcoholic vegetal organs extracts of *Taraxacum officinale*(original photos, Tănasă (Acreței) M.V.)

Obtained hydroalcoholic extracts were analysed by UV-Vis spectrophotometry method for determining flavonoids content; 0.5 mL of extract was diluted in 4 mL water and 8 mL methanol mixture, and absorbance was read against a methanol:water blank at 340 nm wavelength (Szabo et al, 2012; Popoviciu et al, 2020.a; Popoviciu et al, 2020.b).

RESULTS AND DISCUSSIONS

The increased value of the flavonoids concentration in *Taraxacum officinale* was registered for 70:30 (v:v) Flowers ethanol extract, 149864,97±587,45 mg/kg D.W. (Fig. 6) and for whole plant extract, 146641,08±766,23 mg/kg D.W. (Fig. 9)collected from Moldova area, Neamt County, Romania. The decreased content in 50:50 (v:v) Flowers ethanol extract, 25478,66± mg/kg D.W. and 25943,34± mg/kg D.W. Radix in 50:50 (v:v) ethanol extract (Fig. 7) from Transylvania area, Harghita County, Romania, was registered.

Flavonoids content in Taraxacum Flower hydroalcoholic extracts

The higher values of the flavonoids concentration was registered for 50:50 (v:v) and 70:30 (v:v) Flowers ethanol extract collected from Moldova area and the lowest accumulation of the flavonoids was registered in ethanol extracts from plants collected from the area of Transylvania, while for the flowers from Dobrogea area, the content of flavonoids is almost 2,5 time more increased compared to the ones from Transylvania (Fig. 4).

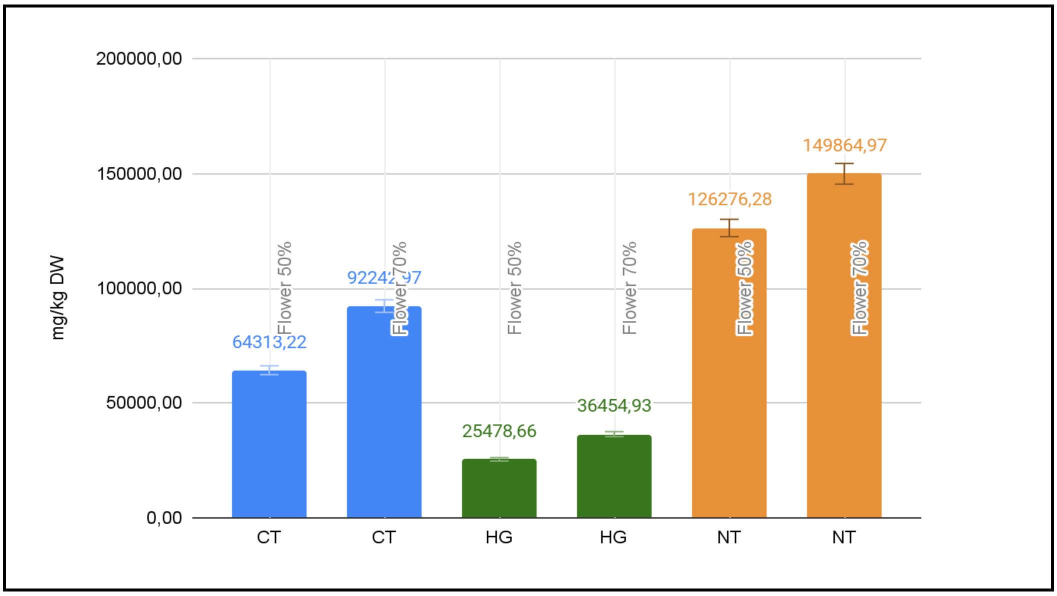

Fig 4. Total flavonoids (mg/kg DW) content in flower hydroalcoholic extracts of *Taraxacum* sp.

Flavonoids content in Taraxacum Radix hydroalcoholic extracts

The comparative values of Radix hydroalcoholic extracts showed a better extraction of the flavonoids in ethanol 50:50 (v:v) concentration for plants collected from Neamt and Constanta Counties, while Harghita County plants had almost similar values of the flavonoids concentration. The flavonoids content of the root hydroalcoholic extracts of *Taraxacum officinale* showed higher values in both extracts of 50:50 (v:v) and 70:30 (v:v) ethanol of plants collected from Moldova region, Radix 50:50 (v:v) revealed almost double amount of flavonoids compared to Radix 50:50 (v:v) ethanol extract from Dobrogea area and this one has approximately double amount of flavonoids compared to Radix 50:50 (v:v) ethanol extract from Transylvania area plants (Fig. 5).

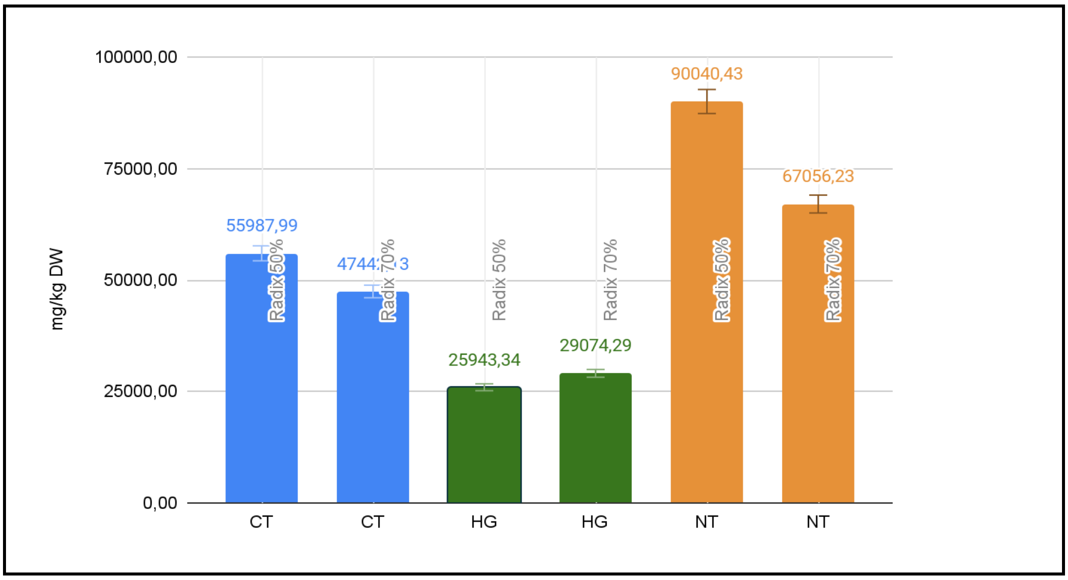

Fig 5. Total flavonoids (mg/kg DW) content in root (coded Radix) hydroalcoholic extracts of *Taraxacum* sp.

Flavonoids content in Taraxacum Herba hydroalcoholic extracts

Herba hydroalcoholic extracts registered higher values of flavonoids concentration compared to Radix, Flower or Mix extracts; Herba 50:50 (v:v) and Herba 70:30 (v:v) ethanol extracts from Neamt County plants had almost the same concentration of flavonoids, more than 135000 mg/kg D.W., pretty close was found the flavonoids concentration Herba 50:50 (v:v) ethanol extract from Constanta County (128177,36 mg/kg D.W.) while the other extracts has more or less half of this concentration (Fig. 6).

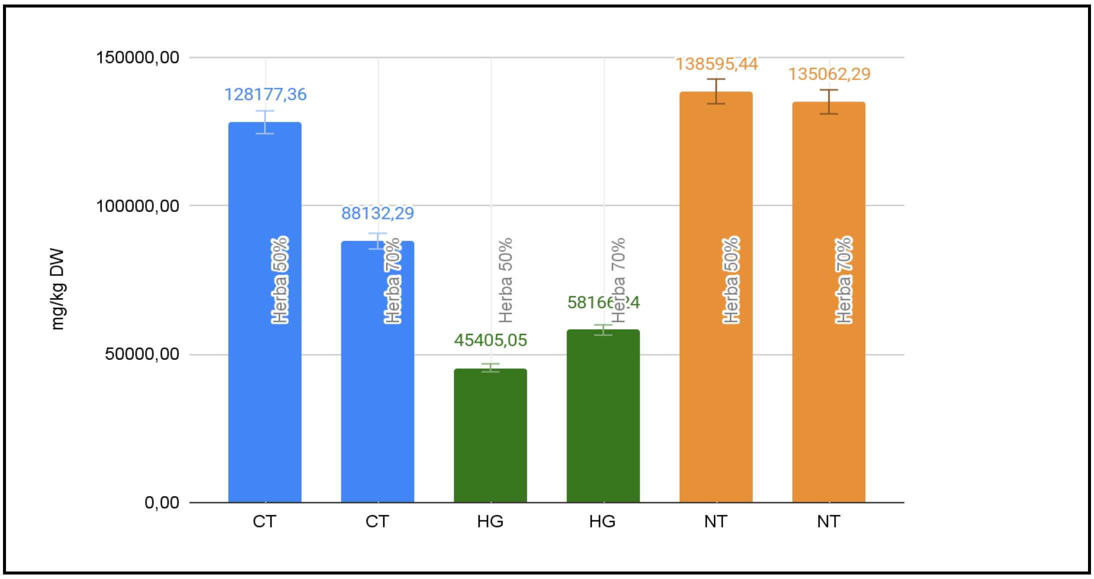

Fig 6. Total flavonoids (mg/kg DW) content in leaves (coded Herba) hydroalcoholic extracts of *Taraxacum* sp.

Flavonoids content in Taraxacum Mix hydroalcoholic extracts

Regarding the content of flavonoids in hydroalcoholic extract of the whole plant (coded Mix), higher values were recorded in 70:30 (v:v) ethanol concentration for all three regions of collected plants. As at the other vegetal organs, the plants from the Moldova region revealed higher content of flavonoids, followed by Dobrogean plants and from Transylvania area (Fig. 7).

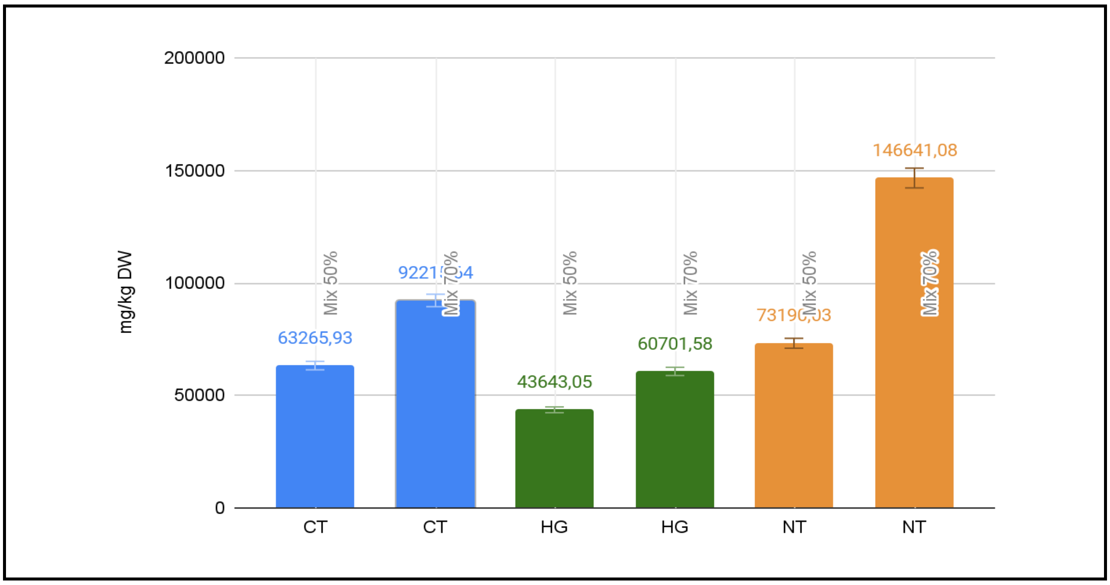

Fig 7. Total flavonoids (mg/kg DW) content in the whole plant (coded Mix) hydroalcoholic extracts of *Taraxacum* sp.

CONCLUSIONS

- The comparative study of the flavonoid content showed that *Taraxacum officinale* (L.) plants collected from Moldova region, Neamt County, Romania, registered the highest flavonoids concentration in all hydroalcoholic extracts obtained from Radix, Herba, Flower and Mix of dandelion plants.
- The highest flavonoid content was demonstrated by Flower hydroalcoholic extracts from plants collected from the Moldova region, Neamt County.
- The lowest flavonoids concentration was revealed in ethanolic extracts of all analysed vegetal organs for the plants collected from the Transylvania area, Harghita County, Romania.
- A better extraction of the bioactive principle of flavonoids was achieved in ethanol of concentration 70:30 (v:v) for plant organs: Flower and Mix for the plants collected from all three regions. At the same time, the hydroalcoholic extracts of Radix and Herba evidenced higher values in 50:50 (v:v) ethanol, for the plants collected from the Moldova and Dobrogea region.
- The particularities of the soil and climate in the geographical areas of Romania: Dobrogea, Moldova and Transylvania upon *Taraxacum* sp. plants determined significantly different values of the concentration of flavonoids and, following these results, the research can be oriented towards the detailed identification of the bioactive components of different plant organs from valuable area and support the possibility to use this valuable Romanian wild flora product for obtaining phytotherapeutic preparations.

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