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Review Article

Literature Review on the Biological Effects of *Taraxacum officinale* Plant in Therapy.

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ABSTRACT

Since human beings have sought in nature, components that can obtain help in therapeutics or even in the cure of diseases. The progress made in the area of science promoted the development of recognized and effective herbal medicines, as well as the search for the population, for less aggressive treatments. The evaluation of the antioxidant activity of plants has been an important issue taking into account its importance on human health, since the natural antioxidants present a reduced health risk, when compared to the synthetic ones that present toxic effect. From the *Asteraceae* family, of which the plant species *Taraxacum officinale*, popularly known as dandelion, stands out among the 71 species on the list of the Ministry of Health (RENISUS), scientifically affirmed, to treat liver disorders, inflammations, potential in the anti-bacterial, cytotoxic, antiviral, antiparasitic, antifungal activity, besides studies to verify its anticancer action and of carcinogenic prevention. The acute toxicity of *Taraxacum officinale* appears to be low, with LD50 values estimated at 36.8g / kg and 28.8g / kg, for the whole plant. The adverse or complex toxic effects for *T. officinale* have not yet been reported. This review of the literature was elaborated through studies of articles contained in the Scielo, Google Scholar and Pub Med platforms. Through this review the importance of phytotherapy studies for pharmacological purposes was verified, aiming to improve the therapeutics.

Keywords: Phytotherapy. *Taraxacum officinale.* Antioxidants. Properties anticancer action.

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INTRODUCTION

From time immemorial, man looks for natural resources to improve his living conditions, increasing in this way, his possibilities of survival, Favoring his health. In all ages and cultures, it retained the use of local natural resources. According to the World Health Organization it is estimated that 80% of the universal population somehow use plant forms to treat diseases [1]. However, it was not known which plants could be or needed to be applied, all based on experimental experiments and scientific information that supported the

elucidation about the beneficial and harmful nature of the products from the vegetal forms in the fight against diseases [2] . With the development of societies, plants have become an important therapeutic resource through man, since they have immeasurable biologically operative substances which enable the synthesis of countless other synthetic substances for the treatment of the various diseases that affect humans [3].With the progress of technology and the recent notions of sustainability that have become common practice since the twentieth century, the use of phytotherapeutic plant forms is increasing worldwide, especially in Brazil due to its enormous vegetal biodiversity, which instigates new studies to in order to obtain new drugs that meet the therapeutic needs and, at the same time, are safe for human health, as well as for all biological areas [3-4].

Among the pharmacological properties studied in natural products are the antioxidant and antimicrobial action. The evaluation of this activity has been an important issue taking into account its importance on human health, since the natural antioxidant agents present low health risk, when compared to the synthetic ones that present toxic effect [5].

Within the environmental sciences, the development of phytotherapeutic drugs stands out because it presents a safe and sustainable alternative, with molecules less environmentally aggressive and that are able to meet the therapeutic needs, without the occurrence of bacterial resistances and persevering chemical residue. In the middle of these various substances, secondary metabolites such as essential oils, tannins, oil-resins and others such as terpenes, flavonoids, saponins, organic acids, and other chemical complexes [6-7] are highlighted in the chemical effect that can be used for countless related researches, since they present diverse properties like anti-inflammatory, antioxidants, anticancer, antimicrobial and several others that contribute to the investigation [8].Some plant forms of the genus *Taraxacum*, known as dandelion, have long been applied in folk medicine to treat liver disorders and some diseases of women, such as breast and uterine cancer, and as infants, choleretics, diuretics and anti- inflammatory drugs [9].This species is listed in the National List of Medicinal Plants of Interest to SUS (RENISUS); a list with a list of phytotherapeutic plant forms that present potential to generate products of interest within the Unified Health System (SUS) and whose purpose is to conduct studies and research that will subsidize the design of a list of herbal and phytotherapeutic plants to be provided for use of the population, safely and effectively for the treatment of a particular disease [10].

From the *Asteraceae* family of which the plant species *Taraxacum officinale*, popularly known as dandelion, has a global distribution, being better expressed in the temperate and subtropical regions, in approximately 1,100 genera and 19,000 species [11].

Among the substances extracted from *Taraxacum officinale* are the terpene derivatives *taraxerol*, *taraxasterol* and the glycoside *taraxacoside*(Figure 1A and B) [12], as well as sterols (ß-sitosterol, stigmasterol), rubber, resins [13], tannins, fatty acids, levulose, a galactose polyholoside and arabinose, caffeic acid, þ-hydroxyphenylacetic acid, asparagine, tyrosine [14], carotenoids, phytosterol, [15], ß-amirin, flavonoids, citric acid, amino acids, saponins and inulin [12].

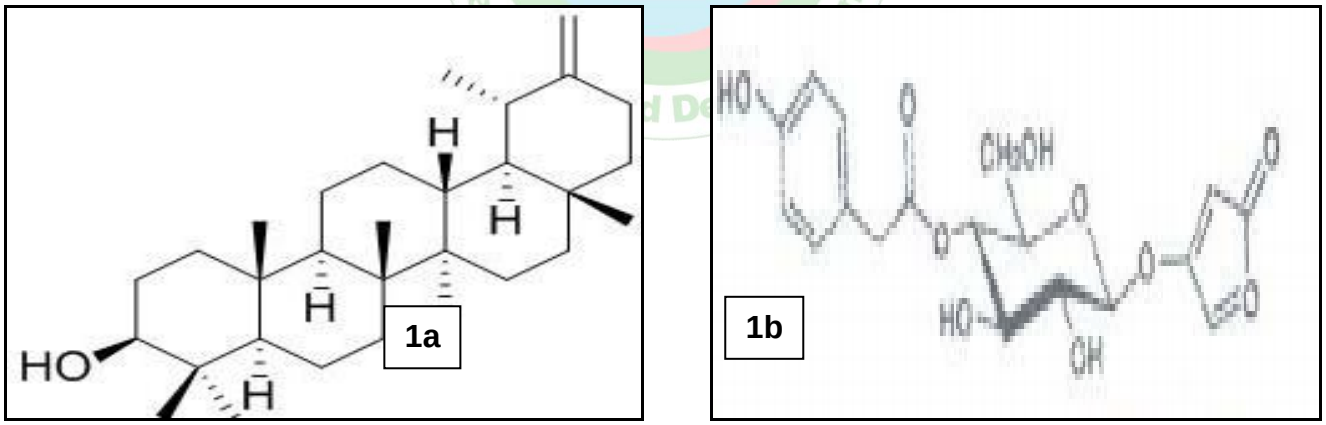

Figure 1: Active principles found in *Taraxacum officinale*. 1a. *Taraxasterol*; 1b.*Taraxacoside*

Regardless of the knowledge and popular application of its phytotherapeutic properties, dandelion was only mentioned in the compendia of therapeutics from the fifteenth century, for its diuretic properties and also as an excellent vulnerary. At the beginning of the 20th century it was strongly used in the so-called taraxocotherapies, being globally commercialized [13].

From the sixteenth century onwards, it became known as a plant drug by apothecaries and was considered one of the safest and most active herbs as a diuretic and one of the best indications for treating liver disorders [12].

In addition to the diuretic properties, the species exhibits slightly laxative properties, stimulating the release of gastric juice, as well as choleretic, collagenous, depurative, antirheumatic and antiscorbic activity. It can be applied against constipation, facial skin diseases (pruritus, eczema, and atherosclerosis), acidosis, headache, jaundice, and uric acid disorders [12-13,15,16].

T. officinale is rich in minerals such as iron, copper and potassium, has the vitamins B1, PP and D[12-14] and contains many more vitamins A (14,000 IU / 100g) and C large majority of vegetables [12-17].

Among the 71 species listed through Ministry of Health, this study is the *Taraxacum officinale*, used by popular wisdom and scientifically affirmed, for hepatic disorders, inflammation, antibacterial activity, respectively[10], as well as studies for to verify its anticancer action and of carcinogenic prevention.

To assure that the *T. officinale* species exerts its therapeutic function without lethally reaching the organism, tests have been made to analyze the toxicity using models based on growing rats, demonstrating disadvantages for the method as the amount of sample expenditure and the high cost. Toxicology studies the effect of established substances on living organisms [18]. The first type of toxicological test to which the compounds are subjected is acute-lethal, consisting of an analysis after short exposure (24h - 48h) of the compound with the bioindicator organism. In toxicology, the median lethal dose (LD50 or LD50) is the required dose of a certain substance or type of radiation to kill 50% of a population under test [usually measured in milligrams of substance per kilogram of body mass of subjects tested (mg / kg = ppm)].

Therefore, the acute toxicity of *Taraxacum officinale* appears to be low, with LD50 values estimated at 36.8g / kg and 28.8g / kg for root and whole plant respectively [19].

In terms of adverse or complex toxic effects for *T. officinale*, they have not yet been mentioned when consumed in the common portions or as food. However, it is worth noting that mild hypotension due to the diuretic effect, as well as contact dermatitis in individuals hypersensitive to latex sesquiterpene lactones have been mentioned [17].

The objective of this article is to present a literature review related to the species *Taraxacum officinale*, in order to present considerations, based on scientific knowledge, related to the biological effects of the plant species.

METHODOLOGY

This article was developed from a literature review on the PubMed, SCIELO, Google Scholar platforms.

The keywords used were "*Taraxacum officinale*", "anticancer", "anti-inflammatory" and "antimicrobial".

After reading the titles of the articles, it was observed that some of them did not meet the study criteria, and these were then excluded from the study. The most relevant articles were selected for reading their abstracts to compose this study. After reading the abstracts, articles were selected that potentially met the criteria originally proposed and read in full.

Criteria For the Eligibility of Scientific Articles

This work aims to demonstrate the importance of studies with phytotherapics, highlighting the *Taraxacum officinale* species, highlighting the advances in antimicrobial, anti -inflammatory, anticancer and anti - carcinogenic therapy. In this context, the articles were selected and grouped into four topics:

a) Antioxidant activity of the plant *Taraxacum officinale* through DPPH methods and micelle mediated extraction.

b) Anti-inflammatory action of *Taraxacum officinale* induced by the inhibition of the production of nitric oxide (NO),which is a pro-inflammatory mediator.

c) Anticancer action of aqueous extracts of *Taraxacum officinale* in the growth and invasion of breast and prostate cancer cells.

d) Antimicrobial action of *Taraxacum officinale*, focusing on antibacterial action for the urinary tract;

DISCUSSION

DPPH is an extremely stable chromophore radical that exhibits absorption peak at the wavelength of 515 nm in methanolic solution, because it has intense violet coloration. As the DPPH is reduced by antioxidant, the electron becomes paired and the absorptivity disappears. Antioxidants that reduce the DPPH radical are characterized as primary. Extract from the leaves of *T. officinale* exhibited significant antioxidant activity. This result confirms the antioxidant activity previously reported for *T officinale*. The antioxidant activity of these extracts seems to be related to the presence of phenolic compounds, such as flavonoids, present in most of the studied species. Phenolic substances such as caffeic acid, chlorogenic acid and luteolin have already been identified in the inflorescences of *T. officinale* and had antioxidant activities tested, but this is the first report of the antioxidant activity of the leaves of this species [20].

In the DPPH test, preparations indicated by high content of hydroxycinnamic acids (HCAs) showed the highest free radical scavenging activity, while others expressed weaker action. However, in blood plasma, the best overall protective effect against H_2O_2/ Fe oxidation was achieved in the presence of enriched fractions of SL amino acid adducts (flavonoids, sesquiterpene lactones) and enriched fraction of inositol 4-hydroxyphenylacetate esters (PIEs), which although not yet described as one of the main components of the dandelion root, was recently discovered as a constituent that presents therapeutic action. None of the dandelion root preparations caused lysis of blood platelets [21].

It was observed that through the micelle-mediated extraction method, all extracts showed excellent anti-radical properties, especially for leaves, as compared to flower samples. Flavonoids derived essentially from luteolin and phenolic acids predominated among certain polyphenols [22].

Some plants of the genus *Taraxacum*, known as dandelion, have long been used in folk medicine for some diseases, most notably those covered in this study such as breast cancer, prostate cancer, as well as its anti-inflammatory and antimicrobial action.

Based on analysis, *Taraxacum officinale* was evaluated as a plant containing anti-inflammatory activity, showing its protective effect against acute pancreatitis induced by cholecystokinin in rats [23].

Nitric oxide (NO) is one of the pro-inflammatory mediators in the pathogenesis of inflammation. Two flavonoid compounds (luteolin and lutein-7-O-glycoside) rich in the ethyl acetate fraction of *Taraxacum officinale* were reported to suppress the production of nitric oxide (NO) and prostaglandin E2 in LPS-activated macrophages

cells, which is attributed to suppression of nitric oxide (iNOS) and cyclooxigenase-2 (COX-2) -induced synthase. It was observed that *Taraxacum officinale* induces apoptosis of human hepatoma HepG2 cells through secretion of tumor necrosis factor (TNF) and interleukin (IL-1) [24].

It has been observed that in primary cultures of rat astrocytes stimulated with LPS and TNF-alpha-inducing substance, *Taraxacum officinale* significantly inhibits the production of TNF by inhibiting IL-1 production, indicating its anti-inflammatory activity in the central nervous system [25].

In addition, it was concluded that other species of the genus *Taraxacum* were characterized as containing several other pharmacological activities. It was also observed that the aqueous extract of *Taraxacum mongolicum* was able to interact with the fluoroquinolines and the antibiotic ciprofloxacin, since it modifies their bioavailability and disposition. *Taraxacum japonicum* exhibited strong antitumor promotion activities in carcinogenesis in two stages of mouse skin tumor induced by a primer and promoter, suggesting its activity [26-27].

In summary, the present work demonstrates that the extract of *Taraxacum officinale* has antiangiogenic, anti-inflammatory and antinociceptive activities, that is, it is also able to reduce NO and COX-2 production and reduce the level of reactive oxygen species (ROS) in activated macrophage cells.

Phytotherapeutic herbs and plants continue to play an expressive role in the discovery and development of drugs, particularly in cancer research. The very significant contribution of natural products to the expansion of the chemotherapeutic arsenal is underlined by the fact that 50% of all anticancer drugs approved globally between 1940 and 2006 were natural products or derived from natural products.

A study of the Evaluation of Aqueous Extracts of *Taraxacum officinale* on the Growth and Invasion of Breast and Prostate Cancer Cells pointed out that the effect of cell proliferation is due to the inhibition of ERK activity, a major determinant of the MARPK pathway involved in cell survival, differentiation and cell growth. The triterpenoids and sesquiterpenes, constituents of the *T. officinale* extract, are responsible for the inhibition of tumor cell proliferation. As these compounds are also present in the roots, and no effect was observed on the growth of any cell line, the results suggest that the inhibitory effect may result from phenolic compounds present in dandelion leaves characterized by polyphenolic acids and flavonoid contents. This is further supported by several studies describing the effect of the latter compounds, in particular polyphenols, on the proliferation of cancer cells [28].

The invasive behavior of tumor cells is another important phenomenon affected by the different *T.officinale* extracts. As demonstrated by the Type I collagen invasion assay, the *T. offcinale* sheet inhibits the invasiveness of the C4-2B LNCaP cells, while no effect could be observed on MCF-7 / AZ cell invasion.

The inhibitory effect of leaf and root of dandelion on the invasiveness of LNCaP cells C4-2B and MCF-7 / AZ, respectively, was evidenced by the zimographic analysis, revealing that the crude extract of leaves and root of tooth- lion cells inhibit the gelatinolytic activity of MMP-2 and MMP-9 (breast cancer cells), since the enzymatic activities of these matrix metalloproteinases correlate with tumorigenicity and metastatic ability of tumor cells. In addition, FAK and src (p-scr) signal transducers contribute to the secretion of matrix metalloproteinases 2 and 9, and activity levels are found high in MCF-7 / AZ invasive cells and in LNCaP C4-2B cells (unpublished data). As a result, it has been found that the anti-invasive effects of the crude leaf and root extracts are mediated by the inhibition of FAK and src activity.

In summary, the data demonstrate that extracts from different parts of *Taraxacum officinale* inhibit cell proliferation and invasion and illustrate the importance of validating the use of traditional medicinal plants and herbs in therapies. In addition, these results indicate that the root and leaf contain active compounds, which can be used in the development of new agents to fight cancer.

When dealing with microorganisms, the most common ones in research are bacteria, in this work alluding to plants with a proven action in the treatment and prevention of infections of the urinary tract, and whose mechanisms of action are better understood in the medicinal plants, giving the highlight was the one used in this study: *Taraxacum officinale*.

The Phytotherapy applied in the treatment of affections of the urinary tract has two central objectives: the treatment of urinary infections and benign prostatic hyperplasia, focusing only on the first situation. Thus, depending on the mode of action of the products based on plant forms used in urinary infections, these can be classified into diuresis promoters and urinary antiseptics, and the diuretic effect is much more important [29].

It is proposed that the diuretic effect be justified as an efficient alternative to provide for the elimination of water, and also to remove bacteria and other infectious agents and nuclei of crystallization of the urinary tract. The diuretic action of these plants is due to the appearance of certain active members, namely: essential oils, flavonoids, saponosides or saponins, minerals and other active compounds such as methylxanthines, cardiotonic glycosides, and others [29].

Because the plant forms contain many components, it is difficult to assimilate their mechanisms of action, since these are generally ill-understood. However, there are some suggestions, such as an increase in the rate of glomerular filtration and an osmotic process (in the case of drugs rich in potassium salts). Plant diuretics are recommended in bacterial and inflammatory affections of the kidneys and urinary tract, such as treatment or prophylaxis in nephrolithiasis and as adjuvants in urinary tract infections.

However, in the case of plant urinary antiseptics, these are recommended for the prophylactic treatment of relapses, following the occurrence of urinary tract infections, mild inflammation of the urinary tract and bladder, and chronic infections (such as urethritis and pyelonephritis) bacteriuria of less than 10^5 microorganisms per ml of urine, since its restricted toxicity and scarcity of side effects make possible its use over long periods of time.

However, these antiseptics have some limitations, such as the fact that their antibacterial activity is not similar to that of antibiotics, which are more effective in the treatment of infections. Thus, when used as a single method of treatment in infections of the urinary tract that occur with fever (acute cystitis), in infections caused by certain pathogens, or when we are in the presence of bacteriuria greater than 10^5 microorganisms per ml of urine, your result may be ineffective.

Although the urinary tract is usually a sterile site, bacteria of the rectum or vagina will have the possibility of migrating and invading this through the urethra [30].

Urinary infection is usually indicative of a count of more than 10^5 microorganisms per ml of urine; however, there are events with symptomatology of an infection, but bacterial counts are less than 10^2 to 10^4 per ml.

The first step in a urinary infection is the colonization of the peri-urethral tissues, followed by the course of the bacteria through the urethra. The next step is the adhesion of the bacteria to the urethra and to the walls of the bladder, followed by proliferation of the same bacteria. Urinary tract infections are caused by microorganisms, especially of bacterial origin, and Gram-negative bacilli are the most common etiological agents. And in most cases, the bacterium *Escherichia coli* is responsible for the infection. It is even thought that *Escherichia coli* is responsible for 85% of urinary tract infections[31-32].

The adhesion of this bacterium is successor by the connection of lectins apparent to the surface of its fimbriae, the carbohydrates in the tissue of the host. Bacteria manifesting several types of fimbriae, it is natural that they also show different binding forces to host tissues. The most virulent *Escherichia coli* bacteria (isolated from patients with pyelonephritis and infections with more urinary tract recurrence), have p-like fimbriae that bind to glycosphingolipids of the renal membrane lipid bilayer, which before the invasion of the renal parenchyma [31-33].

As for the pharmacological activity of Dandelion pointed out that there are studies in annals, demonstrating the diuretic action of the roots of this plant, and this activity is due to the presence of inulin. There is also a study, carried out in individuals, showing that the leaves are responsible for the growth in frequency of urination. The roots and aerial parts of this plant in preclinical studies have also revealed a modulating action of inflammation due to the presence of the sesquiterpene lactones, justifying by all this the use of *Taráxaco* in urinary infections [34].

In addition, he says that the plant of the species *Taraxacum officcinale* has a proven contraindication in case of obstruction of the bile ducts, especially when using the root as a drug, and can only be used in cases of gallstones under medical supervision. Tamoxifen should be used with caution in patients with inflammation of the gastrointestinal tract. In both cases, these contraindications are due to the presence of bitter constituents that can exacerbate these pathological conditions and the possible occurrences of decompensations in patients who take cardiotonics or who are hypertensive, is due to the diuretic action that the root of *Taráxaco* exerts.

CONCLUSION

According to the contextualization of articles and dissertations used as basis for this study, it can be suggested that the plant of the species *Taraxacum officinale* expresses great importance for the advances in phytotherapy medicine, bringing to the fore pharmacological actions of an anti-inflammatory, and antimicrobial, anticancer and carcinogenic prevention.

It is possible to observe that the leaf and root of *Taraxacum officinale* has an anti-inflammatory, anticancer and antimicrobial action that is more significant than the flower of this species.

It is still possible to emphasize that the components of *Taraxacum officinale* are potentiators of some penicillin antibiotics, based on information highlighting the penicillin class antibiotics that are in extinction and in studies still under development, thus allowing a higher yield of these antibiotics, in order to increase its availability in the market, due to the association of this with the extract of the plant *Taraxacum officinale*, thus reducing the amount of penicilinics dispensed per dose, thus, to serve the population for longer.

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