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Diversity of bioactive compounds from *Tropaeolum tuberosum* (mashua)

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Summary

Introduction: *Tropaeolum tuberosum* (mashua), is a member of the *Tropaeolaceae* family, is considered an ecological, millenary crop native in Peru, which began to be consumed in The Andes for having nutritional and medicinal properties. The **objective** of the present literature review is to highlight the importance of mashua as a source of diverse bioactives and to summarize its pharmacological activities. The **method** of the present study is a literature review, where original scientific articles on pharmacological activity and bioactive compounds of mashua were searched in the following electronic databases: PubMed, ScienceDirect and Google Scholar, published during the period 2019 to 2023. **Result**: After the bibliographic search, a total of 22 articles were obtained. It is **concluded** that despite the fact that mashua is attributed several medicinal uses, there are no studies to date that support the efficacy and safety of its use in a pathology. The information presented in this document will be useful to increase the interest and use in the future of the biological compounds of mashua, as well as to give it a new pharmacological or clinical use,

thus, becoming useful for the creation of a new drug formulation in the future, or through the application of the bioactive compounds of mashua in combination with existing drugs to optimize the treatment of pathologies such as cancer, anemia, lithiasis, among others.

Keywords: *Tropaeolum tuberosum*, bioactive compounds, biological activity.

Resumen

Diversidad de compuestos bioactivos de *Tropaeolum tuberosum* (mashua)

Introducción: *Tropaeolum tuberosum* (mashua), es un miembro de la familia Tropaeolaceae, es considerado un cultivo ecológico, milenario, originario del Perú, que comenzó a consumirse en Los Andes por tener propiedades nutricionales y medicinales. El **objetivo** de la presente revisión de la literatura es resaltar la importancia de la mashua como fuente de diversos bioactivos y resumir sus actividades farmacológicas. El **método** del presente estudio es una revisión de la literatura, donde se buscaron artículos científicos originales sobre la actividad farmacológica y compuestos bioactivos de la mashua en las siguientes bases de datos electrónicas: PubMed, ScienceDirect y Google Scholar, publicados durante el periodo 2019 al 2023. **Resultado**: Después de la búsqueda bibliográfica se obtuvo un total de 22 artículos. Se **concluye** que a pesar de que a la mashua se le atribuyen varios usos medicinales, no existen hasta la fecha estudios que avalen la eficacia y seguridad de su uso en alguna patología. La información presentada en este documento será útil para incrementar el interés y uso en el futuro de los compuestos biológicos de mashua, así como para darle un nuevo uso farmacológico o clínico, siendo así de utilidad para la creación de una nueva formulación del fármaco en el futuro, o mediante la aplicación de los compuestos bioactivos de la mashua en combinación con fármacos existentes para optimizar el tratamiento de patologías como cáncer, anemia, litiasis, entre otras.

Palabras clave: Tropaeolum tuberosum, compuestos bioactivos, actividad biológica.

Resumo

Diversidade de compostos bioativos de *Tropaeolum tuberosum* (mashua)

Introdução: *Tropaeolum tuberosum* (mashua), membro da família Tropaeolaceae, é considerada uma cultura ecológica, milenar, nativa do Peru, que começou a ser consumida na Cordilheira dos Andes por possuir propriedades nutricionais e medicinais. **O objetivo** da presente revisão de literatura é destacar a importância do mashua como fonte de diversos bioativos e resumir suas atividades farmacológicas. O método do presente estudo é uma revisão de literatura, onde foram pesquisados artigos científicos originais sobre atividade farmacológica e compostos bioativos do mashua nas seguintes bases de dados eletrônicas: PubMed, ScienceDirect e Google Scholar, publicados durante o período de 2019 a 2023. **Resultado:** Após a pesquisa bibliográfica, obteve-se um total de 22 artigos. **Conclui-se** que apesar de serem atribuídos vários usos medicinais ao mashua, não existem até o momento estudos que sustentem a eficácia e segurança do seu uso em uma patologia. As informações apresentadas neste documento serão úteis para aumentar o interesse e utilização futura dos compostos biológicos do mashua, bem como para dar-lhe um novo uso farmacológico ou clínico, tornando-se assim útil para a criação de uma nova formulação de medicamento no futuro, ou através da aplicação dos compostos bioativos do mashua em combinação com medicamentos existentes para otimizar o tratamento de patologias como câncer, anemia, litíase, entre outras.

Palavras-chave: Tropaeolum tuberosum, compostos bioativos, atividade biológica.

Introduction

Medicinal plants are important resources when it comes to receiving treatment for different pathologies, since they can be used as an alternative or complementary treatment [1]. Conventional treatments are usually good alternatives; however, in the case of certain pathologies or symptomatology, it is recommended to first exhaust some type of non-drug treatment [2]. In addition, pharmacological treatments can lead to dependence, resistance and loss of the sensation of relief when taken for a prolonged period of time [3]. Approximately for the last two decades, there has been a peculiar interest in the use and research of medicinal plants as an alternative to conventional treatments [4, 5]. Despite the strongest criticism of natural therapies such as herbal

medicine is the lack of scientific evidence of efficacy, despite which the use of natural products is increasing in the West, so that herbal medicine has become important worldwide [6, 7].

Mashua (*Tropaeolum tuberosum*) is a tuber considered one of the main food sources worldwide, cultivated in the central zone of the Andes, in countries such as Ecuador, Venezuela, Argentina, Bolivia, Colombia and Peru, where up to 200 morphotypes of this species can be found [8]. This tuber is part of the daily diet of the Andean population and is cooked after being left to rest in the sun in order to obtain a more pleasant flavor [9]. On one side, in Peru, mashua is widely used in the pharmaceutical industry [10]; on the other side, a decrease in the commercialization of mashua has been observed, resulting in low consumer acceptance, especially abroad [11].

An example of an attractive and valuable medicinal plant is mashua (*Tropaeolum tuberosum*), a member of the Tropaeolaceae family. Consequently, researchers have been encouraged to choose plants with medicinal use, to study bioactive compounds and pharmacological activities. The mashua tuber, presents a wide variety of biological properties such as antibacterial, antioxidant, antifungal, anti-inflammatory, etc. In traditional medicine it is used for the treatment of skin diseases, urinary disorders and as diuretic [12, 13]. It has been reported that the mashua tuber has been used until today as a treatment for diseases related to the lungs, kidneys, bladder, skin and even venereal diseases [14]. In fact, the bioactive compounds of mashua have been constantly investigated for their biological activity and chemical compounds, however, the most important data are fragmented and discontinuous. Therefore, the objective of this review is to highlight the importance of mashua as a source of various bioactives and to summarize its pharmacological activities.

Methodology

A literature review was performed by electronic search of original articles in databases such as: PubMed, ScienceDirect and Google Scholar, published during the period 2019 to 2023. The search was performed with the following combined terms: "*Tropaeolum tuberosum*" "medicinal plant", "bioactive compounds" and "biological activities". Studies detailing the chemical composition and biological activity of *Tropaeolum tuberosum* were included, such as: antimicrobial, antioxidant, diuretic, antineoplastic, hypoglycemic, analgesic, and anti-inflammatory, among others.

Results

Table 1 summarizes the main pharmacological indications as well as the chemical components and analytical methods employed.

Table 1. Main chemical components and pharmacological activity

Chemical components under study	Pharmacological activity under study/Instrument
Glucosinolates were identified and quantified in ten mashua cultures.	It was determined whether postharvest cooking and storage techniques affect the stability of glucosinolates and myrosinase activity of Andean mashua tubers. Instrument: UPLC method, UV-visible spectrophotometer, one-way ANOVA and Tukey statistical analysis [11].
Total anthocyanins, total flavonoids, total phenolics, tannin content.	Determination of antioxidant activity. Instrument: AOAC method, Spectrophotometer, ANOVA and Tukey statistical analysis [12].
Horsetail aqueous extract: Flavonoids. Isaño aqueous extract: Tannins, flavonoids and anthocyanins.	Evaluation of diuretic and saliuretic activity. Instrument: Phytochemical screening test, one-way ANOVA statistical analysis and the Bonferroni post-test [13].
Alkamides: → *N*–oleoyldopamine → *N*–(2–Hydroxyethyl)–7Z,10Z,13Z,16Z–docosatetraenamide	Anti-inflammatory activity (Inhibition of TNF-α and NF-kB production in THP-1 monocyte cells). Instrument: TLC technique, column chromatography, FAB ionization technique, cytotoxicity assay, MTT cytotoxicity assay, LDH cytotoxicity assay, TNF-α inhibition assay, NF-kB inhibition assay, ANOVA and Tukey statistical analysis [14] .
Analogues of *N*-benzyl linoleamide, Polyphenols.	Cell viability and anti-inflammatory activity (migraine treatment). Instrument: Nuclear magnetic resonance techniques and mass spectrometry [15].
Glucosinolates, alkamides	Analgesic activity mediated by the transient receptor potential of the vanilloid 1 receptor. Instrument: TLC technique, Spectrophotometry, cytotoxicity assay, MTT viability assay, ANOVA and Tukey statistical analysis [16].

(*Continued*)

Chemical components under study	Pharmacological activity under study/Instrument
2 alkaloid components: → 2-Benzyl-3-thioxohexahydropyrrolo[1,2-c] imidazole-1-one → *N*-(4-acetyl-5-methyl-5-phenyl-4,5-dihydro-1,3,4-thiadiazol-2-yl) acetamide	Cytotoxic activity and capacity for apoptosis. Instrument: Column chromatography, spectroscopy method, ANOVA and Tukey statistical analysis [17]
Carbohydrates, phenolic compounds, anthocyanins, carotenoids, starch and minerals.	Potential sources of bioactive compounds. Instrument: Soxhlet method, Tests to determine pH, Gas Chromatography, HPLC technique, ANOVA and Tukey statistical analysis [18].
Crude fiber, Protein, Vitamin C, Phenolic compounds.	Antioxidant capacity. Instrument: Sensory evaluation through a survey using a 5-point hedonic scale [19].
Macamides isolated from yellow mashua tubers.	Determination of anti-inflammatory activity Instrument: NF-kB inhibition assays, viability and cytotoxicity assays, STAT3 inhibition assays [20].
Phenols, flavonoids, phytosterols, triterpenoids, phytosterols and triterpenoids.	Determination of anti-inflammatory activity Instrument: Gas chromatography-mass spectrometry technique. antioxidant capacity Instrument: Titration technique, Spectrometric method, Pearson correlation coefficient test [21-23].
Anthocyanins, glucosinolates and phenolic compounds.	Anti-inflammatory activity. Instrument: Gas chromatography technique, mass spectrometry, ANOVA and Tukey statistical analysis [24, 25].
High content of polyphenols.	Antioxidant activity, ability to induce detoxifying enzymes and antiproliferative activity. Instrument: Folin-Ciocalteu method, antioxidant capacity assay, glutathione S-transferase assay, quinone oxidoreductase assay, UPLC technique coupled to mass spectrometer, statistical analysis by homogeneity of variances, t-test-, F-test [26-28].
Presence of phenols and flavonoids in three varieties of mashua (pink, yellow and black).	The antioxidant activity was evaluated. Instrument: Phytochemical screening, Folin-Ciocalteu method, aluminum trichloride colorimetric method, mass-coupled gas chromatography method, DPPH method, UV-visible spectrophotometer, Duncan statistical analysis, one-way ANOVA [29].

(*Continued*)

Chemical components under study	Pharmacological activity under study/Instrument
Show significant variation in the basic components of food in the form of energy sources (starch and sugars) or functional elements (essential amino acids, vitamins, FOS, glucosinolates and antioxidants).	Functional foods with healthy properties. Instrument: HPLC technique, ANOVA statistical analysis, LSD test [30].
Presence of monomeric anthocyanins, phenolic compounds in mashua.	Antioxidant capacity. Instrument: Folin-Ciocalteu colorimetric method, DPPH method, Statistical analysis and Least Significant Difference (LMD) test [31].
Non-flavonoid compounds, such as hydroxycinnamic derivatives that represent 100, 26 and 15% of the total phenolic compounds, respectively. Presence of flavan-3-ol monomers. The presence of flavonols was found.	The presence of the compounds and the consideration of the total phenolic content suggest the use of these Andean tubers as promising sources of natural antioxidants widely used in the food industry. Instrument: HPLC-DAD-ESI/MS, Tukey statistical analysis [32].

Use in traditional medicine

Tropaelum tuberosum, also popularly known as mashua, is a tuber widely used as a culinary input by gastronomic professionals worldwide. Likewise, it is also used by farmers and consumed by the high Andean population [15] owing the medicinal properties attributed to it, which can be because of its healing, anti-inflammatory, analgesic, and antioxidant properties [16, 29]. In Andean medicine it was used for the relief of kidney problems [17-19]. Moreover, the high Andean population also used it for liver and skin problems [20] and prostatic affections [31]. Regarding the traditional use of mashua compresses in decoction, it was only for local use to heal skin wounds [16-18, 31]. Finally, it was in pre-Columbian times that the indigenous population used mashua as a treatment for pulmonary, digestive and venereal diseases [16, 17].

Bioactive compounds

The mashua is formed by phytoconstituents such as phenolic compounds [24, 25], fatty acids, alkamides, glucosinolates [2, 21], as well as flavonoids, tannins, anthocyanins and isothiocyanates [18, 21, 24]. The anti-inflammatory property of mashua is due to the presence of macamides, specifically *N*-benzyl linoleamide, which are able to treat soroche also known as altitude sickness [20]. Additionally, there are the alkamides N-oleoyldopamine and *N*-(2-hydroxyethyl)-7Z,10Z,13Z,13Z,16Z-docosatetraenamide, which are also associated with anti-inflammatory effect [14]. On the

other hand, depending on the genotype of the mashua varies the content of phenolic compounds such as anthocyanins, as well as tannins, flavonoids, also contains a large amount of fiber, proteins, carbohydrates, among others [22]. In addition, there are chemical substances such as antioxidant compounds and ascorbic acid [23]. As well as glucosinolates, carotenoids [24].

Several authors indicate that mashua shows the presence of triterpenoids, phytosterols and fatty acids [25]. A study conducted in the province of Cotopaxi in Ecuador, confirmed the amount of total phenolic compounds was 1000 mg gallic acid equivalent (GAE)/100 g dry weight, the total carotenoids was 0.14±0.02 mg/100 g dry weight and anthocyanins 14.0±1.1 mg/100 g dry weight [26]. A second study was also conducted in Ecuador, where phenolic compounds were quantified according to the high-performance liquid chromatography with diode array detection and mass spectrometry detection (HPLC-DAD-ESI/MS^n) technique, finding compounds such as Quercetin-3-O-rutinoside (40.6 µg/g dry matter), kaempferol-O-dirhamnosyl-hexoside (29.5 µg/g dry material (DM)) and kaempferol-O-dihexoside (46.22 µg/g DM), mashua is one of the high Andean plant species, which has been shown to exhibit antineoplastic properties, since in one study the isolated alkaloids produced apoptosis of tumor cells under laboratory conditions [27]. There is also a study that found that total phenolic compounds were found in an amount of 18.27±0.83 ìg GAE/mg of extract by ultra-high performance liquid chromatography-tandem mass spectrometry (UPLC-MS/MS) technique [28, 29].

A study performed in Spain found that Mashua cultivated in Peru had 28.6 ìg/g dry matter of carotenoids, 0.01 mg/g dry matter of anthocyanins and 7.9 mg chlorogenic acid/g dry matter of phenols; while samples from Bolivia had 21.9 ìg/g dry matter of carotenoids, 3.63 mg/g dry matter of anthocyanins and 22.3 mg chlorogenic acid/g dry matter of phenols [30]. Likewise, mashua contain. Another study quantified the glucosinolates (Gls) present in the mashua tuber by means of UPLC coupled to MS, finding amounts of Gls in the range of 4.9-54.2 ìmol/g of dry matter [32].

Pharmacological activities

It has been demonstrated that mashua has biological properties, which can be antibacterial, anti-inflammatory [18], antioxidant, anticancer, including protection of the immune system, due to the presence of isothiocyanate, as well as carotenoids [26], antimicrobial, and even antitumor [14]. In addition, the local population empirically uses this product against skin, pulmonary, venereal and analgesic conditions, among others. In folk medicine, mashua is widely used for its aphrodisiac properties, as well as to alleviate kidney and diuretic problems [18].

It is also used for the treatment of hepatic and metabolic pathologies [22]. It has been reported that the consumption of mashua protects cells from the carcinogenic activity of certain substances, as well as preventing the onset of cardiovascular pathologies [23], in addition to its already known effects against prostate disorders [25].

In the last 5 years, interest in the therapeutic properties of mashua has increased, this is reflected in the variety of in vivo and in vitro scientific studies that have been carried out to confirm its effects, such as its antioxidant and anti-inflammatory activity [22, 25, 28, 31]. As well as publications where they carry out quantification and purification studies of their secondary metabolites, responsible for their pharmacological properties [14, 17, 20, 21]. Many of these studies have raised a molecular basis for these properties, which would justify the consumption of this plant species by the general population. But it has also been shown that it can be consumed in the form of a drink, in which it has been shown that it continues to maintain its most important organic chemical components despite undergoing various manufacturing processes [24]. With this series of evidence, different sectors of the population can be encouraged to consume this tuber, but they must also be educated so that they do not affect the availability of this plant in nature, as well as updated and concise information on its effects on health to avoid inappropriate use. Finally, the different varieties of this species should continue to be investigated because the phytoconstituents may vary depending on the phenotype, as well as their respective therapeutic properties.

Conclusions

This literature review is a brief summary of articles on bioactive compounds and pharmacological activities of mashua, where the therapeutic potential of this medicinal plant is evidenced. The historical aspects of mashua have not fully been addressed because its long history as a traditional medicine is known.

At present, there are no known studies that cover the efficacy of mashua in some ailments. However, there is new research on medicinal properties such as antineoplastic. Due to the diverse spectrum of pharmacological effects that "mashua" presents, studies have been carried out to demonstrate its bioactivity. Each of the constituents have numerous biological properties including anti-inflammatory, analgesic, antioxidant, diuretic and antibacterial.

Several studies have shown that mashua has antimicrobial activity from which a potent antibiotic can be developed, but the biggest problem with mashua is that it is food as such for the culinary and nutraceutical industry, but it is not suitable as an individual component. Research should also be conducted on optimal dosage, efficacy and toxicity

levels. Ultimately, toxicological and clinical trials need to be developed, as mashua is a potent candidate for its main pharmacological activities, which are neoplastic and antibacterial. Likewise, mashua should be used as a complementary treatment, to treat diseases such as cancer, unfortunately there are no studies available that describe its effective use. The present information reported on mashua with respect to its biological activities and chemical compounds will be useful to generate more interest towards mashua and new clinical pharmacological applications can be investigated. Therefore, the present compilation may be useful in formulating new drugs in the future.

Conflict of interest

The authors declare that they have no conflicts of interest to disclose.

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