Review Article

Phytochemistry and Pharmacology of the Genus *Equisetum* (Equisetaceae): A Narrative Review of the Species with Therapeutic Potential for Kidney Diseases

Thaise Boeing, Karyne Garcia Tafarelo Moreno, Arquimedes Gasparotto Junior, Luisa Mota da Silva, and Priscila de Souza

1 Escola de Ciências Farmacêuticas de Ribeirão Preto, Universidade de São Paulo, Ribeirão Preto, São Paulo, Brazil
2 Laboratório de Farmacologia Cardiovascular (LaFuC), Faculdade de Ciências da Saúde, Universidade Federal da Grande Dourados, Dourados, MS, Brazil
3 Programa de Pós-Graduação em Ciências Farmacêuticas, Núcleo de Investigações Químico-Farmacêuticas, Universidade do Vale do Itajaí, Itajaí, Brazil

Correspondence should be addressed to Thaise Boeing; tize.thaise@gmail.com and Priscila de Souza; priscilasouza_rc@yahoo.com.br

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The *Equisetum* genus, Equisetaceae family, is widely distributed worldwide and may be the oldest nonextinct genus on Earth. There are about 30 known species, which are very often used in traditional medicine with diverse applications. This review aimed to compile scientific reports about *Equisetum* species with relevant pharmacological properties and/or therapeutic potential for kidney diseases. Our bibliographic survey demonstrates that the most widespread traditional use of *Equisetum* is as a diuretic, followed by the treatment of genitourinary diseases (kidney diseases, urethritis, kidney stones, and others), inflammation, wound healing, rheumatic diseases, prostatitis, and hypertension. The most popular species from the *Equisetum* genus with medicinal use is *E. arvense* L., whose diuretic effect was confirmed in animal models and clinical trials. The species *E. bogotense* Kunth also demonstrated the beneficial effect of inducing diuresis in both experimental and clinical assays. Several other species have also been studied regarding their therapeutic potential, showing different biological actions. Regarding the chemical composition, it contains many active constituents, such as alkaloids, flavonoids, phenol, phytosterols, saponins, sterols, silicic acid, tannin, triterpenoids, and volatile oils. However, despite the widespread traditional use, many species need to be explored in detail for scientific validation of popular use. Indeed, the species of the *Equisetum* genus have great potential in the management of kidney disorders.

1. Introduction

The genus *Equisetum*, belonging to the Equisetaceae family, from Equisetales order and Equisetopsida class, is a genus of perennial plants that reproduce by spores not seeds, widely distributed worldwide, only absent in Australasia and Antarctica [1, 2]. It may be the oldest nonextinct genus on Earth, originating from the end of the Paleozoic era, about 300 million years ago. There are about 30 known species, with the majority consisting of small plants, which rarely reach a meter in height. Its varied species are adapted to grow in temperate, tropical, and cold regions. They are often used in traditional medicine with diverse applications in many countries, having mainly anti-inflammatory and diuretic activities [3].

The species of *Equisetum* genus are known by the common name of “horsetail” in English-speaking countries, “cola de caballo” in Spanish-speaking countries, “prêle des champs” in France, “ackerschachtelhalm” in Germany, “tsukushi” in Japan, and “cavalinha” in Brazil. Its name is of Latin origin, composed of “equi” (horse) and “setum” (tail), that is, horse tail [4–6]. The most popular species from the
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Equisetum genus with medicinal use is E. arvense L., which has already demonstrated many biological properties, such as antioxidant, antitumoral, antimicrobial, smooth muscle relaxant, anticonvulsant, sedative, anti-anxiety, antinociceptive, anti-inflammatory, anti-diabetic, diuretic, platelet aggregation inhibitory, osteoblastic response promoting, and antileishmanial effects (for review see [7]). However, many other species are also known for their popular usage and common indications for diuretic purposes and kidney disorders, as will be addressed in this review.

For that, this review’s objective was to compile the data found in the literature about Equisetum species with relevant pharmacological properties for the treatment of kidney disorders, especially associated with arterial hypertension. We have collected reports from ethno botanical textbooks, and scientific articles from books and journals indexed online in the databases PubMed (https://www.ncbi.nlm.nih.gov/pubmed), Science Direct (http://www.sciencedirect.com/), and Medline (https://www.nlm.nih.gov/bsd/pmreresources.html). We will discuss popular uses, toxicological data, phytochemical composition, and pharmacological evidence of these species in the next topics. The main findings are summarized in tables for each theme.

2. Traditional Applications and Toxicological Information

Studies that describe this genus’s traditional applications, summarized in Table 1, show that the oral administration is the most common route for its use, using the infusion or decoction of the aerial parts as the main method of preparation [1, 9, 42]. The most widespread traditional use of Equisetum is as a diuretic [1, 12, 33, 34, 41, 42], followed by the treatment of genitourinary diseases (kidney diseases, urethritis, kidney stones, and others) [10, 16, 25, 26, 33, 34, 37–39], inflammation [10, 20–22, 27, 40], wound healing [21, 28, 39, 41], rheumatic diseases [9, 19, 31, 34, 39], prostatitis [33, 36, 40], and hypertension [1, 21, 27].

Studies compiled in this work pointed out that the most popular species from the Equisetum genus with medicinal use is E. arvense L., commonly known as “horsetail”, with uses reported in countries like Brazil, Romania, Germany, Serbia, China, Greece, Portugal, Iran, and Thailand. This species is used mainly as diuretic, to treat inflammation, genitourinary diseases, ulcers, wound healing, dermatitis, hemorrhage, hepatitis, prostatitis, musculoskeletal diseases, and others (Table 1) [12, 20–22, 25, 33, 38, 39, 41, 42]. Nevertheless, Baracho et al. [43] evaluated the acute hepatotoxicity of E. arvense in rats. The extract at 30, 50, and 100 mg/kg did not show mortality in any of the doses at the end of the 14 days of observation, nor did it alter the serum activities of hepatic enzymes compared to the control group. Instead, it produced benign changes in the hepatic morphology. Moreover, Tago et al. [44] evaluated the toxicity of E. arvense in the diet at doses of 0, 0.3, 1, and 3% for 13 weeks in male and female rats. According to the authors, the dosage selections were based on estimated intake for humans, approximately 5 mg/kg daily. No toxicity was detected related to clinical signs, body weight, urinalysis, hematology, serum biochemistry data, organ weights, and histopathological findings. Still, remedies containing E. arvense are not recommended during pregnancy or breastfeeding since little information is available on their safety [45]. Indeed, the species contains thiaminase, an enzyme that destroys thiamine (vitamin B1), and, with long-term use, could lead to vitamin deficiency, a possible cause of neurotoxicity [46].

Another well-cited species is E. telmateia Ehhr., known as “great horsetail” [47], used to treat rheumatism, broken bones, genitourinary diseases, prostatitis, gastrointestinal disorders, inflammation, and hypertension, in addition to its use as diuretic and expectorant in countries like Turkey, Portugal, Iran, and Spain [1, 34, 36, 37, 40]. However, little information is available about its safety. E. giganteum L., commonly called “giant horsetail” [10], is another widespread species mainly in Latin American countries like Brazil, Bolivia, Chile, and Peru, traditionally used to treat diarrhea, heartburn, genitourinary disorders, inflammation, rheumatic diseases, obesity, and as a diuretic [8–11, 18, 28]. Despite its widespread traditional use, no in vitro toxicity studies were conducted so far; however, Alavarche et al. [10] showed no cytotoxic potential of the hydroalcoholic extract of E. giganteum aerial parts (50, 25, 16, 8, and 4 mg/mL) on human palatal epithelial cells and human monocytes using MTT assay.

Similarly to E. giganteum, the species Equisetum bogotense Kunth also grows in Chile, where it is widely used in traditional medicine as a diuretic [48]. As far as we know, there are no cytotoxic studies carried out on animals with this species; however, E. bogotense was subjected to a clinical study where 25 healthy patients received their infusion at an equivalent dose of 0.75 g of the plant per person, daily, for two consecutive days, but no adverse reactions were detected (e.g., diarrhea, asthenia, dizziness, colic, vomiting, palpitations, and hypotension) [18].

Equisetum myriochaetum Schlecht. and Cham. is a plant distributed in Mexico, where it is popularly known as “cola de caballo” [49] and traditionally used for the treatment of diabetes type 2 and kidney disease [14–17]. Regarding toxicological information, Téllez et al. [49] have shown that extracts from E. myriochaetum aerial parts had no acute toxicity detected in Drosophila or in the human microculture test in vitro performed with cultured lymphocytes, emphasizing that this species is not genotoxic.

Moreover, Equisetum debile Roxb. ex Vaucher, also known as “horsetail”, is widely distributed throughout Thailand. The local population has been used as a diuretic, wound muscle relaxant, hair growth stimulant, and anti-hair loss treatment. The E. debile extracts showed no cytotoxicity on dermal papilla cell line (1 to 500 μg/mL) and no irritation on chorioallantoic membrane of hen’s eggs (0.5%) [41], but further studies are needed to ensure their safety.

Equisetum palustre L., known as “marsh horsetail” [50], has been traditionally used in Turkey for peptic ulcer, hemorrhoids, and kidney stones treatment [35]. Despite this, E. palustre has been known for its toxicity for livestock, which is related to the presence of thiaminase and the
| Country     | Species                                      | Plant part          | Preparation method | Medicinal use                                                                 | Reference |
|-------------|----------------------------------------------|---------------------|--------------------|--------------------------------------------------------------------------------|-----------|
| Bolivia     | *Equisetum giganteum* L.                    | Stem, entire plant  | Decoction          | Diarrhea, stomach heat, liver and kidneys diseases, inflammation              | [8]       |
|             |                                              |                     |                    | Rheumatic diseases               | [9]       |
| Brazil      | *Equisetum giganteum* L.                    | Stems\(^a\), aerial parts\(^b\) | Decoction, infusion\(^a\) | Diuretic, urinary disorders, inflammation | [10]      |
|             |                                              |                     |                    | Weight loss\(^a\)           | [11]      |
|             | *Equisetum arvense* L.                      | Aerial parts        | Infusion\(^a\)     | Remineralization, inflammation \(^b\)                                | [12]      |
| Mexico      | *Equisetum myriochaetum* Schlecht and Cham   | Aerial parts        | Infusion\(^a\)     | Diabetes type 2\(^{abc}\)                                      | [13]      |
|             |                                              |                     |                    | Kidney diseases, diabetes\(^d\)                      | [14]      |
|             | *Equisetum* arvense L.                      | Aerial parts        | Infusion\(^a\)     | Anti-inflammatory               | [15]      |
|             |                                              |                     |                    | Sugar lowering                   | [16]      |
|            | *Equisetum* arvense L.                      | Aerial parts        | Infusion\(^a\)     | Antirheumatic, antineuralgic          | [18]      |
|             |                                              |                     |                    | Diuretic                        | [19]      |
| Lebanon     | *Equisetum* arvense L.                      | Aerial parts        | Decoction          | Diarrhea, diuretic, emmenagogue, wound healing | [20]      |
|             |                                              |                     |                    | Inflammation\(^ab\)               | [21]      |
| Romania     | *Equisetum arvense* L.                      | Sterile aerial, stems | Unreported         | Ulcers, skin tumors, itching, wound healing, bruise, chilblains, leukorrhea, paronychia, foot hyperhidrosis, impetigo, furuncle, dermatitis, neurodermatitis | [22]      |
| Germany     | *Equisetum arvense* L.                      | Aerial parts        | Unreported         | Urogenital diseases, diuretic\(^a\)                                      | [23]      |
| Serbia      | *Equisetum arvense* L.                      | Whole plant\(^a\), sterile stems\(^b\) | Infusion         | Kidney diseases, arthritis, bleeding ulcers, tuberculosis, wounds healing\(^b\) | [24]      |
| China       | *Equisetum arvense* L.                      | Aerial parts        | Unreported         | Hemorrhage, urethritis, jaundice, hepatitis                                  | [25–27]   |
|             | *Equisetum hyemale* L.                      | Aerial parts        | Unreported         | Hypertension, inflammation, acute stroke, bleeding, cancer                   |           |
| Peru        | *Equisetum giganteum* L.                    | Aerial parts        | Unreported         | Hemorrhage, urethritis, jaundice, hepatitis                                  |           |
| Colombia    | *Equisetum* bogotense Kunth                 | Whole plant         | Infusion, decoction | Diarrhea, diuretic, emmenagogue, wound healing | [28]      |
| India       | *Equisetum arvense* L.                      | Aerial parts        | Infusion           | Diuretic, kidney stones                                                        | [29]      |
| Italy       | *Equisetum arvense* L.                      | Aerial parts        | Infusion           | Strengthen bones, hair, nails                                               | [30]      |
| Croatia     | *Equisetum arvense* L.                      | Aerial parts        | Infusion           | Remineralizing, diuretic, inflammation, rheumatoid arthritis                  | [31]      |
| Greece      | *Equisetum arvense* L.                      | Aerial parts        | Decoction          | Diabetes                                                                        | [32]      |
| Turkey      | *Equisetum telmateia* Ehrl.                 | Aerial parts        | Decoction          | Urogenital disorders, prostatitis, diuretic, musculoskeletal diseases         | [33]      |
|             | *Equisetum palustre* L.                     | Aerial parts        | Infusion           | Acne, rheumatism, broken bones, diuretic, expectorant, kidney stones, strengthening hair, skin, and nails |           |
| Portugal    | *Equisetum telmateia* Ehrl.                 | Aerial parts        | Unreported         | Peptic ulcer, hemorrhoids, kidney stones                                      | [34, 35]  |
|             | *Equisetum arvense* L.                      | Aerial parts        | Unreported         | Prostatitis, stomachaches, and cystitis\(^a\)                             | [36]      |
|             |                                              |                     |                    | Urinary, kidney, gastrointestinal disorders\(^b\) | [37]      |
|             | *Equisetum telmateia* Ehrl.                 | Aerial parts        | Unreported         | Arthritis, kidney diseases, bleeding ulcers, hepatitis, jaundice, and tuberculosis | [38]      |
| Iran        | *Equisetum arvense* L.                      | Aerial parts        | Unreported         | Wound healing, strengthening of the bones, teeth, nails, and hair, gout, nosebleeds, urinary and prostate disorders, menorrhagia, rheumatoid arthritis | [39, 40]  |
| Thailand    | *Equisetum arvense* L.                      | Aerial parts        | Unreported         | Prostatitis, stomachache, inflammation, diarrheaa, mouth infections, chronic eczema, anti fungal |           |
|             | *Equisetum telmateia* Ehrl.                 | Aerial parts        | Unreported         | Hair loss                                                                       |           |
|             | *Equisetum debile* Roxb. ex Voucher         | Aerial parts        | Unreported         | Diuretic, wound healing, muscle relaxant, hair growth stimulant, hair loss    |           |
| Spain       | *Equisetum telmateia* Ehrl.                 | Aerial parts        | Infusion\(^a\)     | Hypertension, diuretic\(^a\)                                                |           |
|             | *Equisetum arvense* L.                      | Aerial parts        | Decoction, infusion\(^ab\) | Bone disorders, to strengthen broken bones\(^b\) |           |
|             | *Equisetum ramosissimum* Desf.              | Aerial parts        | Infusion\(^a\)     | Hypertension, diuretic\(^a\)                                                |           |
|             |                                              |                     |                    | Bone disorders, to strengthen broken bones\(^b\) |           |

Equal letters in the same line relate plant part, preparation method, and medicinal use to respective studies (column of references).
alkaloids palustrine and nicotine [50]. Besides, Milovanović et al. [24] showed that *E. palustre*, as well as *E. arvense* L., *E. sylvaticum* L., *E. fluviatile* L., and *E. telmateia* Ehrh. extracts (62.5 μg/ml), showed some genotoxicity, presenting a higher incidence of micronucleus formation than that of the control.

3. Phytochemistry Data of *Equisetum* Genus

In this topic, we reviewed the phytochemistry data available on the plants’ species of *Equisetum* genus (Table 2), which have already been presented for their traditional applications. Chemical structures of the compounds identified in the *Equisetum* genus followed by their names, molecular weights, and references are shown in Figure S1 (Supplementary Material).

*E. arvense* L. contains various chemical compounds such as silicic acid, linoleic acid, oleic acid, stearic acid, linolenic acid and traces of alkaloids (e.g., equisetin, nicotine, palustrine, and palustrinin), glucoside, flavonoids, saponosides, triterpenoids, phytosterols, calcium carbonate, potassium sulfate, potassium chloride, manganese chloride, iron, manganese, and calcium phosphate [39, 52]. Indeed, Veit et al. [51] isolated two styrylpyrone glucosides (3′-deoxyequisetumpyrone and 4′-O-methylequisetumpyrone) from the MeOH extract from the rhizomes of *E. arvense*. Besides, in the hepatoprotective activity-guided fractionation of the MeOH extract from the aerial parts of *E. arvense* L. performed by Oh et al. [25], the bioactive EtOAc fraction was subjected to octadecyl-functionalized silica gel flash column chromatography resulting in the isolation of two phenolic petrosins (onitin and onitin-9-β-D-glucopyranosyl)oxy[megastigm-7-ene-3,5,6-triol. Moreover, Gründemann et al. [22] have also focused on the *E. arvense* extract’s phytochemical analysis on identifying flavonoids and other polar phenolics. A decoction produced by boiling a part of dry plant material with nine parts of ethanol for 4 h was subjected to the HPLC method to separate the phenolic compounds in the extract later identified by liquid chromatography-mass spectrometry (LC-MS). The major constituents were mono-, di-, and triglycosides of kaempferol, quercetin, apigenin, genkwanin, and protogenkwanin as well as mono- and dicaffeoyl-tartaric acid. Besides, three phenolic glycosides, equisetumoside A, equisetumoside B, and equisetumoside C, were isolated from the water-soluble extract of fertile sprouts of *E. arvense*, together with uridine, inosine, 2′-deoxyinosine, 2′-deoxycytidine, tryptophan, thymidine, 5-carboxy-2′-deoxyuridine, coniferin, and kaempferol 3-O-β-D-sophoroside-7-O-β-D-glucopyranoside, by Chang et al. [54].

As described in the clinical study conducted by Lemus et al. [18], only a few chemical screenings have been published in the late 1980s and early 1990s demonstrating the presence of β-sitosterol, silicic anhydride, flavonoids, and coumarins, as well as isokaempferide and kaempferol derivatives in *E. bogotense* HBK. Besides, more recently, Tipke et al. [56] identified and quantified the alkaloids present in this species by hydrophilic interaction liquid chromatography high-performance liquid chromatography tandem mass spectrometry (HILIC HPLC-MS/MS) in electrospray ionization (ESI). The plant material was powdered using a standard electric coffee grinder and submitted to alkaloids extraction using sulphuric acid. The presence of nicotine, palustrine, and palustridiene was detected; however, only two out of five samples were positive for the compounds. Therefore, the authors stated that more data is necessary to have a clearer picture of the occurrence of alkaloids in this species.

Xu et al. [58] reported the isolation and characterization of three new megastigmane glucosides and four known constituents from the whole plant of *E. debile*. The dried whole plant of *E. debile* was extracted with CHCl₃ and 70% EtOH. After solvent evaporation, the EtOH extract was partitioned with AcOEt and BuOH, subjected to column chromatography (CC). The AcOEt fraction afforded blumenol A and corchusinoside C, while BuOH-soluble extract afforded sammanigoside A, debilosides A–C, and (3S,5R,6R,7E,9S)-9-[(β-D-glucopyranosyl)oxy]megastigm-7-ene-3,5,6-triol. Moreover, Tan et al. [57] investigated this plant’s chemical constituents obtaining 12 compounds. The whole dried plant of *E. debile* was powdered, extracted with EtOH, and posteriorly partitioned. The EtOAc fraction yielded the new phenylhexane debiliol, the new alkaloid asetinum, guaicylglycerol-β-coniferyl ether, and the compounds 5-hydroxymethyl-2-furfuraldehyde, coumaric acid, p-hydroxybenzoic acid, and the hydroalcoholic extract of *E. arvense* sterile stems was also characterized by Milovanović et al. [24]. The authors have found the nonmalonylated quercetin 3-O-glucoside and the free aglycone quercetin as the major constituents, but quercetin 3-O-(6′-O-malonylglucoside), 5-O-caffeoyl shikimic acid, monocaffeoyl-meso-tartaric acid, and dicaffeoyl-meso-tartaric acid were also detected. Besides, Gründemann et al. [22] have also focused on the *E. arvense* extract’s phytochemical analysis on identifying flavonoids and other polar phenolics. A decoction produced by boiling a part of dry plant material with nine parts of ethanol for 4 h was subjected to the HPLC method to separate the phenolic compounds in the extract later identified by liquid chromatography-mass spectrometry (LC-MS). The major constituents were mono-, di-, and triglycosides of kaempferol, quercetin, apigenin, genkwanin, and protogenkwanin as well as mono- and dicaffeoyl-tartaric acid. Besides, three phenolic glycosides, equisetumoside A, equisetumoside B, and equisetumoside C, were isolated from the water-soluble extract of fertile sprouts of *E. arvense*, together with uridine, inosine, 2′-deoxyinosine, 2′-deoxycytidine, tryptophan, thymidine, 5-carboxy-2′-deoxyuridine, coniferin, and kaempferol 3-O-β-D-sophoroside-7-O-β-D-glucopyranoside, by Chang et al. [54].
Table 2: Phytochemistry of *Equisetum* genus stratified by species, plant part, method, and compounds.

| Species          | Plant part | Extract/method            | Compounds                                                                 | Reference |
|------------------|------------|---------------------------|---------------------------------------------------------------------------|-----------|
| *Equisetum arvense* L. | Rhizomes   | MeOH/CC-HPLC              | 3′′-Deoxyequisetumpyrone                                                   | [51]      |
|                  |            |                           | 4′′-O-Methylequisetumpyrone                                                |           |
|                  |            |                           | Onitin                                                                     |           |
|                  |            |                           | Onitin-9-O-glucoside                                                       |           |
|                  |            | EtOAc fraction/CC         | Apigenin                                                                   | [25]      |
|                  |            |                           | Luteolin                                                                   |           |
|                  |            | EtOAc fraction/HPLC-DAD   | Kaempferol 3-O-glucoside                                                   |           |
|                  |            |                           | Quercetin 3-O-glucoside                                                    |           |
|                  |            |                           | Quercetin 3-O-glucoside                                                    |           |
|                  |            | n-ButOH fraction/HPLC-DAD | Apigenin 5-O-glucoside                                                     | [52]      |
|                  |            |                           | Kaempferol 3-O-glycoside                                                   |           |
|                  |            |                           | Quercetin 3-O-glycoside                                                    |           |
|                  | Aerial parts| EtOAc fraction/HPLC-DAD   | Di-3′′-caffeoyl-meso-tartaric acid                                          |           |
|                  |            |                           | Di-3′′-caffeoyl-meso-tartaric acid                                          |           |
|                  |            | H₂O fraction/HPLC-DAD     | Phenolic acid 1                                                            |           |
|                  |            |                           | Phenolic acid 2                                                            |           |
|                  |            | Petrol/PTLC-GC-MS         | Taraxerol                                                                  |           |
|                  |            |                           | β-amyrin                                                                   |           |
|                  |            |                           | Germanicol                                                                 |           |
|                  |            |                           | α-Amyrin                                                                   |           |
|                  |            |                           | Ursolic acid                                                               |           |
|                  |            |                           | Oleanolic acid                                                             |           |
|                  |            |                           | Betulinic acid                                                             |           |
|                  |            |                           | Isobaueranol                                                               | [53]      |
|                  |            |                           | Epicholestanol                                                             |           |
|                  |            |                           | Cholesterol                                                                |           |
|                  |            |                           | Sitosterol                                                                 |           |
|                  |            |                           | 28-Isofuscoester                                                          |           |
|                  |            |                           | Taraxasterone                                                             |           |
|                  |            |                           | Ψ-Taraxasterone                                                           |           |
|                  |            |                           | Mono-, di-, and triglycosides of kaempferol                               |           |
|                  |            | Unreported Ethanol decoct/HPLC | Apigenin                                                                  | [22]      |
|                  |            |                           | Genkwanin                                                                  |           |
|                  |            |                           | Protophenkwanin                                                            |           |
| Fertile sprouts  |            | Water-soluble/spectroscopic analysis | Equisetumosis A-C                                                          |           |
|                  |            |                           | Uridine                                                                    |           |
|                  |            |                           | Inosine                                                                    |           |
|                  |            |                           | 2′′-Deoxyerythrose                                                       | [54]      |
|                  |            |                           | 2′-Deoxyxuridine                                                           |           |
|                  |            |                           | Tryptophan                                                                |           |
|                  |            |                           | Thymidine                                                                  |           |
|                  |            |                           | 5-Carboxy-2′′-deoxyuridine                                                 |           |
|                  |            |                           | Coniferin                                                                  |           |
|                  |            |                           | Kaempferol 3-O-β-D-sophoroside-7-O-β-D-glucopyranoside                    |           |
|                  |            |                           | Quercetin 3-O-glucoside                                                    |           |
| Stems            |            | Hydroalcoholic/HPLC       | Quercetin 3-O-(6′′-O-malonylglucoside)                                     | [24]      |
|                  |            |                           | 5-O-Caffeoyl shikimic acid                                                |           |
|                  |            |                           | Monocaffeoyl meso-tartaric acid                                           |           |
|                  |            |                           | Dicaffeoyl meso-tartaric acid                                             |           |
|                  |            |                           | Benzaldehyde                                                               |           |
|                  |            |                           | Phenylethanal                                                              |           |
|                  |            |                           | 2-Phenylethanol                                                            |           |
|                  |            |                           | 4-Vinylguaiacol                                                            |           |
|                  |            |                           | Isovanillin                                                                |           |
|                  |            |                           | Homovanillic acid                                                          |           |
|                  |            |                           | 2,3-Octanedione                                                            |           |
|                  |            |                           | Hexanoic acid                                                              |           |
|                  |            |                           | (Z)-3-Hexanoic acid                                                        |           |
|                  |            |                           | (E)-2-Hexanoic acid                                                        |           |
|                  |            |                           | Dihydroactinidiolide                                                       |           |
|                  |            |                           | (E/Z)-Pseudoionone                                                         |           |
|                  |            |                           | (E,E)-Pseudoionone                                                         |           |
|                  |            |                           | 3-Hydroxy-β-ionone                                                         |           |
|                  |            |                           | 4-Hydroxy-β-ionone                                                         |           |
|                  | Aerial parts|                     | 3-Oxo-α-ionol                                                              | [55]      |
|                  |            |                           | 3-Hydroxy-7,8-dihydro-β-ionone                                            |           |
|                  |            |                           | 3-Hydroxy-7,8-epoxy-β-ionone                                               |           |
|                  |            |                           | 4-Oxo-β-ionone                                                             |           |
|                  |            |                           | 4-Hydroxy-7,8-dihydro-β-ionone                                             |           |
| Species                  | Plant part | Extract/method                     | Compounds                                                                 | Reference |
|--------------------------|------------|-------------------------------------|---------------------------------------------------------------------------|-----------|
| *Equisetum bogotense* Kunth | Unreported | Acidic/HILIC HPLC                  | Nicotine, Palustrine, Palustridien, Phenylethane debiltiliol, Equisetmine | [56]      |
|                          |            | EtOAc/CC                            | Guaiacylglycerol-β-comiferyl ether, 5-Hydroxymethyl-2-furfuraldehyde, Coumaric acid, p-Hydroxybenzoic acid, Ferulic acid, (+)-Lariciresinol 9-O-β-D-glucopyranoside 8-O-4′-Neolignan glucoside debilignanoside | [57]      |
|                          | Whole plant| BuOH/CC                             | Equisetumoside B, (+)-Isolariciresinol-3-a-O-β-D-glucopyranoside Thymidine, Blumenol A, Corchoinoside C, Sammangaoside A, Debilosides A–C | [58]      |
| *Equisetum debile* Roxb. ex Vaucher |            | BuOH/CC                             | (3S,5R,6S,7E,9S)-Megastigman-7-ene-5,6-epoxy-3,9-diol 3,9-O-β-D-glucopyranoside (6R,9S)-3-Oxo-α-ionol 9-O-β-D-glucopyranoside Debiloside B | [59]      |
|                          | Aerial parts| MeOH/CC                             | Kaempferol 3-O-sophoroside, Kaempferol 3,7-O-β-D-diglucopyranoside, Phenylethyl O-β-D-glucopyranoside, (Z)-3-Hexanyl O-β-D-glucopyranoside (7S,8R)-Dehydrodiconiferyl 4-O-β-D-glucopyranoside L-tryptophan, Quercetin tri-O-hexoside, Kaempferol 3-O-sophoroside-7-O-glucoside, 3-Hydroxyhispidin 3,4′-di-O-glucoside, Quercetin 3,7-di-O-glucoside, Quercetin 3-O-(caffeoyl) glucoside | [60]      |
|                          | Stems      | Hydroethanolic/LC-DAD and LC–ESI-MS/MS | Kaempferol 3,7-di-O-glucoside, Flavonol-di-O-hexoside, Equisetumprone, Caffeic acid derivative, Kaempferol 3-O-sophoroside, Ferulic acid derivative, Kaempferol 3-O-glucoside, Kaempferol 3-O-sophoroside-7-O-glucoside, 3-Hydroxyhispidin 3,4′-di-O-glucoside, Quercetin 3,7-di-O-glucoside, Quercetin 3-O-(caffeoyl) glucoside, Kaempferol 3,7-di-O-glucoside, Flavonol-di-O-hexoside, Equisetumprone, Caffeic acid derivative, Kaempferol 3-O-sophoroside, Ferulic acid derivative, Kaempferol 3-O-glucoside | [10]      |
| *Equisetum giganteum* L. | Aerial parts| Hydroethanolic/HP-LC, UV–Vis, and MS/MS | Kaempferol 3,7-di-O-glucoside, Flavonol-di-O-hexoside, Equisetumprone, Caffeic acid derivative, Kaempferol 3-O-sophoroside, Ferulic acid derivative, Kaempferol 3-O-glucoside | [56]      |
|                          | Unreported  | Acidic/HILIC HPLC                   | Palustridienne                                                             | [56]      |
| Species                  | Plant part | Extract/method               | Compounds                                                                 | Reference |
|-------------------------|------------|------------------------------|---------------------------------------------------------------------------|-----------|
| Equisetum hyemale L.    | Aerial parts | Hydroalcoholic/HPLC-PAD       | Gallic acid                                                               | [61]      |
|                         |            |                              | Tannic acid                                                               |           |
|                         |            |                              | Chlorogenic acid                                                          |           |
|                         |            |                              | Caffeic acid                                                              |           |
|                         |            |                              | Quercetin                                                                 |           |
|                         |            |                              | Kaempferol 7-O-β-D-glucopyranoside                                        |           |
|                         |            |                              | a-D-fructofuranose                                                        |           |
|                         | n-BuOH/CC  | 5-Hydroxymethylfurfural      | L-Uridine                                                                 | [62]      |
|                         |            |                              | Kaempferol 3.7-di-O-β-D-glucopyranoside                                   |           |
|                         |            |                              | Kaempferol 3-sophoroside-7-O-β-D-glucopyranoside                           |           |
|                         |            |                              | Kaempferol 7-O-α-L-rhamnoside-4′-O-β-D-glucopyranoside                     |           |
|                         | Aerial parts | H₂O and BuOH/CC-HPLC         | Kaempferol 3-O-sophoroside-4-O-β-glucoside                                | [63]      |
|                         |            |                              | Caffeoyl-methylate-4-β-glucopyranoside                                    |           |
| Equisetum myriochaetum  | Unreported | Acidic/HILIC HPLC            | Chrysin                                                                   | [64]      |
| Schlecht. and Cham.     |            |                              | β-D-glicosylstilosterol                                                    |           |
|                         |            |                              | β-D-glucose                                                               |           |
|                         |            |                              | Fatty acids                                                               |           |
|                         |            |                              | Nicotine                                                                  |           |
|                         | Unreported | Acidic/HILIC HPLC            | Palustrine                                                                | [56]      |
|                         |            |                              | Palustridenede                                                            |           |
|                         | Whole plant | Acidic fraction/HPLC-ESI-MS/MS | Palustridene                                                             |           |
|                         |            |                              | N²-Formylpalustrine                                                       |           |
|                         |            |                              | N²-Acetylpalustrine                                                       |           |
|                         | Aerial parts | n-BuOH/HS-CCCC               | 18-Deoxypalustrine                                                        | [50]      |
|                         |            |                              | Palustridieni                                                             |           |
|                         |            |                              | Myricidine                                                                |           |
|                         |            |                              | Spermidine                                                                |           |
| Equisetum palustre L.   | Stems      | Hydroalcoholic/HPLC           | Kaempferol 3-O-glucoside                                                  | [24]      |
|                         | Aerial parts | Diethyl ether/GC-MS          | Kaempferol 3'-O-rutinoside                                                |           |
|                         |            |                              | Kaempferol 3-O-rutinoside-7-O-sophoroside                                 |           |
|                         |            |                              | Kaempferol 3-O-rutinoside-7-O-glucoside                                   |           |
|                         |            |                              | Monocaffeoyl meso-tartaric acid                                           |           |
|                         |            |                              | Benzaldehyde                                                              |           |
|                         |            |                              | Phenylethanal                                                             |           |
|                         |            |                              | 2-Phenylethanol                                                           |           |
|                         |            |                              | 4-Vinylguaiacol                                                           |           |
|                         |            |                              | Isovanillin                                                               |           |
|                         |            |                              | Homovanillic acid                                                         |           |
|                         |            |                              | 2,3-Octanediene                                                           |           |
|                         |            |                              | Hexanoic acid                                                             |           |
|                         |            |                              | (Z)-3-Hexanoic acid                                                       |           |
|                         |            |                              | (E)-2-Hexanoic acid                                                       |           |
|                         |            |                              | Dihydroactinidiolide                                                      |           |
|                         |            |                              | (E,E)-Pseudoionone                                                         |           |
|                         |            |                              | (E,Z)-Pseudoionone                                                         |           |
|                         |            |                              | 3-Hydroxy-β-ionol                                                         |           |
|                         |            |                              | 4-Hydroxy-β-ionol                                                         |           |
|                         |            |                              | 3-Oxo-α-ionol                                                             |           |
|                         |            |                              | 3-Hydroxy-7,8-dihydro-β-ionol                                            |           |
|                         |            |                              | 3-Hydroxy-7,8-epoxy-β-ionol                                              |           |
|                         |            |                              | 4-Oxo-β-ionone                                                            |           |
|                         |            |                              | 4-Hydroxy-7,8-dihydro-β-ionol                                            |           |
ferulic acid. In contrast, the compounds (+)-lariciresinol 9-O-β-D-glucopyranoside, 8-O-4′ neolignan glucoside debiligenoside, equisetumoside B, (+)-isolariciresinol-3a-O-β-D-glucopyranoside, and thymidine were obtained from BuOH fraction. Besides, Kanchanapoom et al. [59] described the isolation of chemical constituents from the MeOH extract from aerial parts of E. debile, including megastigmane glucosides (macarangioside D, sammangooside A, (3S, 5R, 6S, 7E, 9S)-megastigman-7-ene-5,6-epoxy-3,9-diol 3-O-β-D-digluco-pyranoside, (6R,9S)-3-oxo-a-ionol 9-O-β-D-glucopyranoside, and debiloside B), flavonoid glycosides (kaempferol 3-O-sophoroside, kaempferol 3-O-(6″-O-acetylglucoside)-7-O-rhamnoside, kaempferol 3-O-β-D-glucopyranoside-7-O-rhamnoside), and proanthocyanidins (procyanidin dimer B2, procyanidin dimer C1).

### Table 2: Continued.

| Species             | Plant part | Extract/method                  | Compounds                                                                                   | Reference   |
|---------------------|------------|----------------------------------|---------------------------------------------------------------------------------------------|-------------|
| Equisetum ramosissimum Desf. | Aerial parts | Diethyl ether/GC-MS              | Phenylethanal, 2-Phenylethanol, Phenylacetic acid, (Z)-Ferulic acid, (E)-Ferulic acid, (E)-2-Heptenal  | [55]        |
|                     |            |                                  | Hexanoic acid, Heptanoic acid, (E,Z)-2-decenal, Nonanoic acid, (E,E)-2,4-Decadienal, (E,E)-2,4-Decadienal |             |
|                     |            |                                  | Lauric acid, 3-Hydroxy-7,8-epoxy-β-ionol, Kaempferol 3-O-glucoside, Kaempferol 3-O-(6″-O-acetylglucoside) |             |
|                     |            |                                  | Proanthocyanidin tetramer containing an Afz residue, Caffeic acid derivative, A-type proanthocyanidin trimer | [24]        |
|                     |            |                                  | Proanthocyanidin trimer (epi)Afz-(epi)C-(epi)C-(epi)Afz                                    | [36]        |
| Stems               | Hydroalcoholic/HPLC |                          | Kaempferol 3-O-glucoside, Kaempferol 3-O-(6″-O-acetylglucoside)-7-O-glucoside, Kaempferol 3-O-(6″-O-acetylglucoside)-7-O-rhamnoside |             |
|                     |            |                                  | Proanthocyanidin tetramer containing two Afz residues, Caffeic acid derivative, Kaempferol glucose-oside-rhamnoside |             |
|                     |            |                                  | Caffeic acid derivative, Kaempferol acetylglucoside-rhamnoside, Kaempferol 3-O-glucoside, Benzy alcohol |             |
| Equisetum telmateia Ehrh. | Aerial parts | EtOAc fraction/HPLC-PAD-ESI/MS | Proanthocyanidin trimer (epi)Afz-(epi)C-(epi)C-(epi)Afz, Caffeic acid derivative | [55]        |
|                     |            |                                  | Kaempferol acetylglucoside-rhamnoside, Kaempferol 3-O-glucoside, Kaempferol 3-O-acetylglucoside |             |
|                     |            |                                  | Proanthocyanidin tetramer containing two Afz residues, Caffeic acid derivative, Kaempferol glucose-oside-rhamnoside |             |
|                     |            |                                  | Caffeic acid derivative, Kaempferol acetylglucoside-rhamnoside, Kaempferol 3-O-glucoside, Benzy alcohol |             |
|                     |            |                                  | (Z)-3-Hexanoic acid, β-Caryophyllene, α-ionone, (E,E)-Pseudoisonone, 3-Oxo-7,8-dihydro-α-ionone |             |
|                     |            |                                  | 3-Hydroxy-α-ionone, 3-Oxo-α-ionol, 3-Hydroxy-7,8-epoxy-β-ionol, 4-Hydroxy-7,8-dihydro-β-ionol |             |

Afzelechin (Afz); column chromatography (CC); gas chromatography (GC); epicatechin or catechin ((epi)C); epiafzelechin or afzelechin ((epi)Afz); high-performance liquid chromatography (HPLC); high-speed centrifugal countercurrent chromatography (HS-CCCC); diode-array detector (DAD); hydrophilic interaction chromatography (HILIC); liquid chromatography (LC); electrospray ionization (ESI); mass spectrometry (MS); reversed-phase ultra-high-performance liquid chromatography (RP-UHPLC); pulsated amperometric detection (PAD); ultraviolet–visible spectroscopy (UV-Vis); preparative thin layer chromatography (PTLC).
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kaempferol 3-O-sophoroside-7-O-β-D-glucopyranoside), a phenylethanoid glucoside (phenethyl O-β-D-glucopyranoside), an aliphatic glucoside (Z)-3-hexenyl O-β-D-glucopyranoside), a neoglycan glucoside (7S, 8R)-dehydromiconiferyl 4-O-β-D-glucopyranoside), and amino acid (L-tryptophan).

Francescato et al. [60] have evaluated the phenolic composition of the hydroalcoholic extract of E. giganteum stems by LC-DAD and LC-ESI-MS/MS allowing the characterization of 12 compounds (Table 2). Caffeic acid derivatives, flavonoids, and styrylpyrones were detected; in addition, the phenolic components quercetin-3-O-(cafeoyl)-glucoside and 3-hydroxyhispidin-3,4′-di-O-glucoside were reported for the first time in the Equisetum genus, while the most abundant flavonoids were kaempferol derivatives. Similarly, Alavarce et al. [10] identified 13 constituents in the hydroalcoholic extract from the aerial parts of E. giganteum by reversed-phase ultra-high-performance liquid chromatography (RP-UHPLC), ultraviolet–visible spectroscopy (UV-Vis), and MS/MS spectra analysis, also detecting styrylpyrones and flavonoid glucosides derivatives of quercetin and kaempferol. Moreover, the alkaloid palustridene was the only one found in this species in the plant’s acid extract in the study conducted by Tipke et al. [56].

The hydroalcoholic extract from aerial parts of E. hyemale L. was characterized by Queiroz et al. [61] by spectrophotometric and HPLC methods with pulsed amperometric detector (PAD) analyses. Phenolic compounds were detected and identified as gallic acid, tannic acid, chlorogenic acid, and caffeic acid. Moreover, Jin et al. [62] identified 9 compounds in the n-BuOH fraction obtained from EtOH extract of E. hyemale aerial parts by CC. The authors obtained 8 known compounds, with kaempferol-3-sophoroside-7-O-β-D-glucopyranoside and kaempferol-7-O-α-L-rhamnoside-4′-O-β-D-glucopyranoside being first reported to be isolated from this plant, and a new phenyl glycoside, (2-(sophorosyl)-1-(4-hydroxyphenyl) ethanone).

Regarding E. myriochaetum, the compounds kaempferol-3-O-sophoroside, kaempferol-3,7-di-O-β-glucoside, kaempferol-3-O-sophoroside-4′-O-β-glucoside, and caf-feoyl-methylate-4′-β-glucopyranoside were isolated by Wiedenfeld et al. [63] and Cetto et al. [66] from the water-soluble portion of the aerial parts of this species. Besides, Camacho et al. [64] also isolated the constituents pino-cembrin, chrysin, β-sitosterol, β-D-glucosylsitosoterol, β-D-glucose, and fatty acids.

As mentioned before, Tipke et al. [56] analyzed the alkaloids present in Equisetum species using HILIC-HPLC-ESIpos-MS/MS approach. Interestingly, the highest levels of alkaloids were detected in E. palustre samples (close to 1 g alkaloid per kg), which were mainly dominated by palustrine and palustridene. Similarly, Cramer et al. [50] screened twenty-two E. palustre samples by the same method. Although the alkaloids’ content and distribution suffered variability, palustrine and palustridene were the main compounds found as well. In addition, another four palustrine-like and three palustridene-like alkaloids were detected, but only four of them were identified, being N5-formylpalustrine, N5-acetylpalustrine, 18-deoxypalustrine, and N5-formylpalustridene. Moreover, two related compounds were detected (myricidine and spermidine). Nevertheless, in the bioassay-guided fractionation study using ethanol (EtOH)-induced ulcer model in rats, Gurbuz et al. [35] have obtained, by high-speed centrifugal countercurrent chromatography (HS-CCCC) technique, three fractions from the n-BuOH extract of the aerial parts of E. palustre, identifying for the first time in this species the compound kaempferol 3-O-1′-β-D-glucopyranosyl-3-O-1″-β-D-glucopyranoside. Posteriorly, Wei et al. [65] have also isolated this compound, together with 4-O-({p-coumaryl})shikimic acid, luteolin-7-O-β-D-glucopyranoside, quercetin-3-O-β-D-glucopyranoside, apigenin-5-O-β-D-glucopyranoside, genkwanin-5-O-β-D-glucopyranoside, luteolin, apigenin, and genkwanin using MSPD extraction and UHPLC–MS/MS. It was also observed that the content of flavonoid was markedly higher than that of flavonoid aglycones. Milovanović et al. [24] studied the hydroalcoholic extract from the sterile stems of this species as well. The predominant constituents were kaempferol glycosides, such as kaempferol 3-O-rutinoside-7-O-sophoroside, kaempferol 3-O-rutinoside-7-O-glucoside, and kaempferol 3-O-glucoside, but other compounds were detected in smaller amounts.

Interestingly, in the same abovementioned study, the HPLC profile of E. telmateia hydroalcoholic extract of the sterile stems showed predominance of kaempferol 3,7-O-diglucoside and 5-O-caffeoyl shikimic acid; however, a relatively high content of acetylated flavonoid derivatives such as kaempferol-3-O-(6′″-O-acetylglucoside), kaempferol 3-O-(6′″-O-acetylglucoside)-7-O-glucoside, and kaempferol 3-O-(6′″-O-acetylglucoside)-7-O-rhamnoside has been found, so far exclusively, in this species of the genus. Regarding the aerial parts of E. telmateia, analysis of the aqueous extract and the ethyl acetate fraction by HPLC-PAD-ESI/MS performed by Correia et al. [36] allowed the identification of major phenolic compounds such as flavan-3-ol, kaempferol, and phenolic acid derivatives. Retention characteristics and UV spectra also allowed the identification of protocatechuc and p-hydroxybenzoic acids and the presence of various caffeic acid derivatives. Further identities assigned to the ethyl acetate fraction compounds from the infusion of E. telmateia are displayed in Table 2.

Finally, in the previously mentioned study carried out by Fons et al. [55] on the volatile profile of fresh aerial parts of Equisetum species, E. palustre showed forty-four volatile organic compounds, mostly lipidic derivatives (1-octen-3-ol, (E)-2-hexenoic acid) and odorous compounds ((E)2-hexenal, (Z)-3-hexenol, hexanol, and (E)-2-nonenal), while linalool was the only terpenic derivative identified. E. telmateia was dominated by a large number of isoprenoid derivatives (3-hydroxy-7,8-epoxy-β-ionol and 3-hydroxy-a-ionone) as well as one benzenic derivative (3-methoxy-4-hydroxyxystrene, also called 4-vinylguaicol). The major volatile constituents in E. hyemale derived from the lipidic pathway ((E)-2-heptenyl) and shikimic pathway (E)- and (Z)-ferulic acid isomers, 4- vinylguaicol, and isovanillin), while E. ramosissimum showed the highest amount of shikimic derivatives ((E)-ferulic acid, 4-vinylguaicol, (Z)-
ferulic acid, and 2-phenylethanol), but other studies on the chemical composition of the last species mentioned have not been found.

4. Pharmacological Potential of \textit{Equisetum} Genus

4.1. Species with Therapeutic Potential for Kidney Diseases.

Carneiro et al. [13] described the diuretic effect of a standardized dried extract of \textit{E. arvense} (EADE) by monitoring 36 healthy male volunteers’ water balance. Through four repeated days, the authors administered EADE (900 mg/day), placebo (corn starch, 900 mg/day), or hydrochlorothiazide (25 mg/day), separated by a 10-day washout period. The \textit{E. arvense} extract was able to significantly induce diuresis similar to the hydrochlorothiazide group, without triggering important variations in the elimination of electrolytes. The clinical checkups and laboratory assessments showed no changes before or after the test, suggesting that the extract of \textit{E. arvense} is safe for acute use. However, despite the promising results described herein, further research is required to elucidate its diuretic action mechanism.

The ability of the ethanol extract from the roots of \textit{E. arvense} to impact the urinary bladder activity in rats was studied by Zhang et al. [67], by treating them with a standard diet containing 0.2% of the extract. After 3 weeks, cystometry with 0.2% acetic acid solution was done and bladder activity was recorded; in addition, blood pressure, body weight, and adenosine triphosphate (ATP) were measured before and after the stimulation. The control group results showed that during cystometry with acetic acid, the time interval between urinary bladder contractions was shorter, and maximum bladder contraction pressure was much greater. In contrast, the changes observed were lower in the \textit{E. arvense} group. Furthermore, the plasma adrenaline and noradrenaline levels were reduced in the \textit{E. arvense} group compared to the control group. Besides, the increase in the levels of urinary ATP was smaller in rats treated with \textit{E. arvense} extract compared to the control group. Therefore, it was demonstrated that the ethanolic extract of root from \textit{E. arvense} influences urinary bladder activity and can treat urinary bladder disorders.

Gažová et al. [68] performed a clinical study designed to evaluate the efficacy and security of CELcomplex, a preparation comprising a mix of \textit{Cucurbita pepo} L. seed extract, \textit{Equisetum arvense} L., and \textit{Linum usitatissimum} L., on stress urinary incontinence in female patients recruited from 20 urological and gynecological patient clinics in Slovakia. Interestingly, after 12 weeks of treatment (625 mg, two pills for the first 14 days and one pill daily until the end of the treatment), the patients presented a 30% improvement in urinary incontinence episodes, 40% improvement in day-time urination frequency, and 64% gain in nocturnal urination frequency. However, some side effects were reported, including headache, flatulence, and gastrointestinal discomfort. Indeed, further studies may be needed to determine each plant’s isolated effect in this combination and the effectiveness and efficacy of this phytotherapy in other populations.

Recently, the diuretic efficacy of another herbal mixture containing \textit{E. arvense} was also evaluated clinically. Perna et al. [69] assessed the effectiveness of 4 and 8 weeks of supplementation with highly standardized formula, with \textit{Fraxinus ornus} L. plus \textit{Ananas comosus} L., \textit{Betula pendula} R., \textit{Equisetum arvense} L., \textit{Urtica dioica} L., and \textit{Pilosella officinarum} L. Vaill. dry extract, on the state of hydration and bloating sensation in subjects with high and moderate extracellular water. In this study, 19 women with extracellular water over 45% completed the study and their data were analyzed at baseline, at 30 and 60 days. Bioimpedance, short form with 36 questions, and anthropometric parameters were assessed. The extracellular water decreased at 30 and 60 days, as well as the fat mass. Improvement of free fat mass was measured but not on the bloating sensation survey at 60 days. Again, similarly to Gažová et al. [68], further studies may be needed to determine each plant’s isolated effect and the efficacy of this herbal mix in other populations.

Another study evaluating the botanical formulation containing \textit{Herniaria glabra} L., \textit{Agropyron repens}, \textit{Equisetum arvense} L., and \textit{Sambucus nigra} L. was undertaken to explore the preventive role of this combination in an experimental model of nephrolithiasis induced by the oral treatment with 0.75% ethylene glycol (EG) and 1% ammonium chloride for three days, followed by 15 days with only EG. The groups received different doses of the formulation, ranging from 30 mg/kg to 500 mg/kg. The results revealed that the group treated with 125 mg/kg of the formulation had a significant lower calcium oxalate crystals deposits amount when compared with the placebo-only treated group. All the doses significantly diminished the quantity of microcalcifications and reduced the number of kidneys affected by subcapsular fibrosis. Besides, the doses of 125 mg/kg and 500 mg/kg were able to induce diuresis. Although the study has not explored the effects of the species in isolation, this formulation’s potential is evident and significant [70]. Indeed, more studies are needed to investigate the mechanisms responsible for the effect and the safe use of these preparations.

Although the main purpose of this review is to discuss the scientific findings of the different \textit{Equisetum} species, it is important to mention that some compounds isolated from these species have already revealed beneficial actions regarding their ability to induce diuresis. In this context, the flavonoid luteolin, found in the aerial parts of \textit{E. arvense} and \textit{E. palustre}, induced both diuretic and natriuretic effect in normotensive and hypertensive rats, without interfering with urinary pH, K+, or Cl− levels. This study also showed the involvement of muscarinic acetylcholine receptors for luteolin renal effects [71]. Besides, the diuretic activity of isoquercitrin (quercetin 3-O-glucoside), a compound also found in \textit{E. arvense} aerial parts, was studied by Gasparotto et al. [72]. The flavonoid showed diuretic activity in a 7-day repeated-dose study in spontaneously hypertensive rats (SHR). Isoquercitrin (10 mg/kg, p.o.) increased Na+ excretion and presented K+-sparing effects similar to spironolactone. Those effects were related to angiotensin-converting enzyme inhibition; increased bioavailability of bradykinin, PGI2, nitric oxide; and inhibitory effect on renal Na+/K+-ATPase activity.
Moreover, the treatment with oleanolic acid (3β-hydroxy-olea-12-en-28-oic acid) at 60 mg/kg/day for 4 weeks has demonstrated antihypertensive effect in L-NAME-induced hypertension in rats by promoting diuresis and increasing Na⁺ excretion compared to the L-NAME group, in addition to inducing nephroprotection [73].

Extracts from *E. giganteum* and *E. bogotense* have demonstrated a diuretic activity in laboratory animals [18, 48]. Further, the diuretic activity of *E. bogotense* was also evaluated in healthy volunteers through their water balance by Lemos et al. [18]. In addition to biochemical parameters, such as urinary electrolyte concentration, urine density, osmolarity, and pH value, clinical observations on arterial pressure and any adverse reactions were also determined. A 10% *E. bogotense* infusion showed a significant diuretic effect in healthy subjects compared to the control group. Besides, none of the volunteers reported any evidence of adverse reaction, nor did they show any change in blood pressure. Urinary electrolytes showed a significant increase in Na⁺, K⁺, and Cl⁻ excretion compared to the control group, but inside the usual physiological values. Despite the great variation in diuresis excretion levels of the subjects, the study results suggest that an infusion of *E. bogotense* could be used to induce diuresis. As mentioned before, little information is available regarding the chemical composition of this species; only the alkaloids nicotine, palustrine, and palustridiene were identified. Of those, nicotine was described as anti-diuretic [74], while the other alkaloids’ effect remains unknown.

Gutiérrez et al. [75] proved that the chloroform extracts of some species of *Equisetum* genus, including the *E. fluviatile*, *E. hyemale* var. *affine*, *E. giganteum*, and *E. myriochaetum*, at dose of 50 mg/kg, presented acute diuretic activity in CD1 strain mice using hydrochlorothiazide, spironolactone, and furosemide as standard drugs for comparison (given at a dose of 25 mg/kg). It was found that the most active plant was *E. hyemale* var. *affine*, followed by *E. fluviatile*, *E. giganteum*, and *E. myriochaetum*, producing an effect similar to hydrochlorothiazide in relation to the excretion of Na⁺, K⁺, and Cl⁻. Besides, gallic acid, found in the aerial parts of *E. hyemale*, also exhibited a diuretic effect when orally given to normotensive and hypertensive rats, an effect associated with increased Na⁺ and Cl⁻ levels in the urine. This study also showed the endogenous prostanooid generation’s involvement in the renal effects induced by gallic acid [76]. Moreover, caffeic acid, found in the species *E. giganteum*, *E. hyemale*, and *E. telmateia*, induced diuresis in normotensive rats, associated with an increased urinary Na⁺ and K⁺ elimination and a urinary Ca²⁺-sparing effect. In agreement with these findings, this study also demonstrated, by using an *in vitro* assay of urinary calculus formation, that the caffeic acid reduced the number of the monohydrate and dihydrate forms of calcium oxalate crystals formed in the urine, suggesting the diuretic plus antiurolithic effect of this compound [77]. On the other hand, it is important to mention that kaempferol, a compound found in many species of the *Equisetum* genus, was studied by Cechnel-Zanchet et al. [78], but did not present diuretic action.

A last compound of interest found in the species *E. giganteum*, *E. ramosissimum*, and *E. debile* is ferulic acid, which has been reported as nephroprotective in a great number of studies conducted on animals. This phenolic acid has been shown to reduce liver and renal oxidative damage induced by cadmium [79], as well as hyperglycemia [80], lipopolysaccharide [81], or methotrexate [82] induced kidney nephrotoxicity by attenuating inflammation process and reducing oxidative stress. For instance, Alam et al. [83] have shown that chronic treatment with ferulic acid (50 mg/kg) also reduced systolic blood pressure of SHR animals and Wistar rats receiving L-NAME for 8 weeks. This compound was able to reduce left ventricular diastolic stiffness and attenuate inflammatory cell infiltration, ferric iron accumulation, and collagen deposition in left ventricles and kidneys in both models of hypertension. Moreover, ferulic acid improved both endothelium-dependent relaxation in isolated thoracic aortic rings and antioxidative balance in the heart and kidneys. Finally, we can suggest that these compounds, at least in part, seem to contribute to the pharmacological effects described by these species. However, many compounds have not yet been the subject of studies that specifically target these biological activities, so there is a fruitful field to be explored in the future.

5. Other Properties of Pharmacological Interest

Do Monte et al. [84] described the antinociceptive and anti-inflammatory effects of hydroalcoholic extract of stems from *E. arvense* in mice. Briefly, the results of the present study demonstrated that the extract exhibits an antinociceptive effect in chemical models of nociception. In agreement with these results, Steinbor et al. [85] verified the anti-inflammatory properties of *E. arvense* through its silica content, revealing that silica-rich horsetail preparations suppress lymphocytes’ activation and proliferation by an interleukin-2-dependent mechanism and a downregulation of interferon gamma (IFN-γ). Interestingly, analytical profiling by HPLC-UV-MS and bioactivity testing revealed significative immunosuppressive concentrations of a component that was identified as isoquercetin. Thus, the authors concluded that both silica and isoquercitrin are active compounds of horsetail preparations. The anti-inflammatory and antinociceptive effects of *E. arvense* have also been investigated in clinical studies. In one of them, five herbs (including *E. arvense*) plus thiamine reduced the pain and improved functional mobility in patients with pain [86]. The complex of 5 herbs, plus vitamin B1, was well tolerated. The results suggest that the blend should be considered a valuable alternative treatment in managing chronic musculoskeletal pain. However, the exact contribution of *E. arvense* in these clinical results still needs to be quantified.

*E. arvense* has also been described as a promising source of anticancer compounds and its ethanol extract showed a cytotoxic effect on HeLa (cervical cancer cells), HT-29 (colorectal adenocarcinoma), and MCF7 (breast cancer) cell line [87]. Moreover, Alexandru et al. [88] reported that the
| Effect                              | Key findings                                                                 | Species                                                                 | Reference               |
|------------------------------------|-----------------------------------------------------------------------------|------------------------------------------------------------------------|-------------------------|
| **Diuretic activity**              | Increased excretion of sodium, potassium, and chloride                      | Equisetum fluviatile                                                   | [75]                    |
|                                   |                                                                             | Equisetum hyemale var. affine                                           |                         |
|                                   |                                                                             | Equisetum giganteum                                                   |                         |
|                                   |                                                                             | Equisetum myriochaetum                                                |                         |
|                                   | Increased excretion of sodium, potassium, and chloride*                     | Equisetum bogotense                                                   | [18]                    |
|                                   | No effects on the urinary excretion of electrolytes*                        | Equisetum arvense L.                                                  | [13]                    |
| **Urinary bladder disorders**      | Increased interval between urinary bladder contractions and decreased bladder contraction pressure | Equisetum arvense L.                                                  | [67]                    |
| **Urinary incontinence**          | Improved in urinary incontinence episodes; day-time urination frequency; and gain in nocturnal urinary frequency* | CELcomplex® (Cucurbita pepo L.; Equisetum arvense L.; and Linum usitatissimum L.) | [68]                    |
| **State of hydration and bloating sensation** | Decreased extracellular water and fat mass*                              | Formula (Fraxinus ornus L.; Ananas comosus L.; Betula pendula R.; Equisetum arvense L.; Urtica dioica L.; and Pilosella officinarum L. Vaill.) | [69]                    |
| **Nephrolithiasis**               | Lower calcium oxalate crystals                                             | Equisetum arvense L.                                                  | [84]                    |
|                                   | Inhibitory action on chemically induced acute pain test                     | Antidiabetic                                                          |                         |
| **Antinociceptive effect**         | Reduction of clinical chronic musculoskeletal pain*                        | Equisetum arvense L.                                                  | [86]                    |
| **Anti-inflammatory effect**       | Anti-inflammatory action on COPD model                                      | Equisetum arvense L.                                                  |                         |
|                                   | Reduction of antigen-induced arthritis model                              | Antimicrobial                                                          |                         |
| **Cytotoxic and anticancer effect**| Reduction in cell viability of cancer cells                                | Equisetum arvense L.                                                  | [87–90]                 |
| **Effect on bone diseases**        | Increase in calcium absorption                                             | Equisetum arvense L.                                                  | [92]                    |
|                                   | Proliferation of osteoblasts or inhibitory action in osteoclasts            | Equisetum arvense L.                                                  | [38, 94]                |
|                                   | Bone resorption markers of rats                                             | Equisetum arvense L.                                                  |                         |
|                                   | Bone mineral density of rats                                               | Equisetum arvense L.                                                  |                         |
|                                   | Beneficial effects in streptozotocin-induced diabetic rats                  | Antioxidant and antimicrobial                                          |                         |
|                                   | Clinically beneficial to recently diagnosed type 2 diabetic patients*       | Equisetum arvense L.                                                  |                         |
| **Antidiabetic**                   | Beneficial effects in alloxan-induced diabetic rabbits                      | Antioxidant and antimicrobial                                          |                         |
|                                   | Reduction in oxidative stress                                              | Equisetum arvense L.                                                  |                         |
|                                   | Antimicrobial activity                                                     | Equisetum arvense L.                                                  |                         |
|                                   | Antioxidant and antimicrobial of supercritical fluid extraction             | Equisetum arvense L.                                                  |                         |
|                                   | Bactericidal, fungicidal, and antiprotozoal effect                         | Antioxidant and antimicrobial                                          |                         |
|                                   | Bactericidal and fungicidal activity                                       | Equisetum arvense L.                                                  |                         |
| **Antioxidant and antimicrobial**  | Radical scavenger activity                                                 | Antioxidant and antimicrobial                                          |                         |
|                                   | Radical scavenger activity and antimicrobial activity                       | Equisetum arvense L.                                                  |                         |
|                                   |                               | Equisetum sylvaticum L.                                                |                         |
|                                   |                               | Equisetum fluviatile L.                                                |                         |
|                                   |                               | Equisetum palustrae L.                                                 |                         |
|                                   |                               | Equisetum telmateia Ehrh.                                              |                         |
| **Effects on central nervous system** | Prolonged the ketamine-induced total sleeping time and decreased the locomotor activity in mice | Antioxidant and antimicrobial                                          |                         |
| **Antiulcer**                      | Gastroprotective potential against different ulcerogenic agents              | Antioxidant and antimicrobial                                          |                         |

*Clinical study.
aqueous extract from sterile stems of *E. arvense* exerted concentration dependent cytotoxic effects on human leukemic cells (U937 cells). The results from Al Mohammed et al. [89] demonstrated that the ethanolic extract of *E. arvense* presented cytotoxicity and decreased the cell viability of adenocarcinomic human alveolar basal epithelial cells (A549 cells). Recently, Bhat et al. [90] studied the cytotoxic and suppressive action of the ethanolic extract of *E. arvense* against human pancreatic carcinoma cell line ASPC-1. The extract showed potential cytotoxicity and reduced the cellular proliferation of these cells. Similarly, a very strong antimicrobial action of volatile constituents of *E. arvense* was reported by Radulović et al. [91] against the bacteria *Staphylococcus aureus*, *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, and *Salmonella enteritidis* and the fungi *Aspergillus niger* and *Candida albicans*. Remarkably, the essential oil of *E. arvense* is shown to possess a broad spectrum of a robust antimicrobial activity against all tested strains.

*E. arvense* for the treatment of osteoporosis has been extensively studied, mainly because it contains a substantial quantity of silica and its ingesting leads to the absorption and use of calcium and the formation of collagen [92]. Besides, it contains several secondary metabolites that help prevent bone loss caused by age and estrogen deficiency [93]. Furthermore, the osteoblasts’ proliferative effects of *E. arvense* together with its inhibitory action in osteoclasts functions have also been described [38, 94]. Corroborating these results, Kotwal and Badole [95] confirmed the beneficial effects of an extract of *E. arvense* on the bone mineral density of rats submitted to ovariec-tomy. Finally, Arbabzadegan et al. [96] also confirmed these *E. arvense* extract effects by analyzing the mandibular bone mineral density from rats.

*E. giganteum* has been traditionally used as an antidiabetic herbal remedy to treat diabetes. Recently, Vieira et al. [97] investigated the antidiabetic effects of the butanolic and aqueous extracts from *E. giganteum* in an animal model of diabetes. Both aqueous and butanolic extracts could significantly reduce glucose, cholesterol, and triacylglycerol, thus demonstrating their hypolipidemic and hypoglycemic effects. *E. giganteum* has also been intensively studied with the aim of preventing oral diseases because some studies showed its antimicrobial action [10, 28, 98]. Also, despite the use of *E. giganteum* as a diuretic medicinal plant, Farinon et al. [9] evaluated the effect of its aqueous extract as immunomodulatory therapy in a model of antigen-induced arthritis (AIA). The treatment with the extract reduced nociception at 3, 6, and 24 h, decreased leukocyte migration, and inhibited lymphocyte proliferation. In conclusion, it was confirmed that *E. giganteum* extract has an anti-inflammatory and immunomodulatory potential in the acute inflammation model.

Studies in streptozotocin-induced diabetic rats showed that water and butanol extracts of the aerial parts of *E. myriochaetum* have significant hypoglycemic activity in an animal model [66]. Revilla et al. [99] also described the hypoglycemic effect of *E. myriochaetum* through a clinical trial. Type 2 diagnosed diabetic patients were analyzed and received a single dose of the extract significantly reduced the patients’ blood glucose levels, proving a promising potential of this species in the therapeutic management of diabetic individuals.

Yeganegi et al. [40] evaluated *E. telmateia* extracts’ antimicrobial activity against *Staphylococcus aureus*, *Bacillus cereus*, *Escherichia coli*, *Salmonella typhi*, and *Candida albicans*. The results of this group of authors showed that the extract of *E. telmateia* exhibited the highest antimicrobial potency against *S. aureus*. Besides, regarding the antimicrobial potential of another species, *E. hyemale*, two articles were found. The first was contributed by Queiroz et al. [61], who showed an antifungal activity of the extract against dermatophyte fungi (*Trichophyton rubrum* and *Microsporum canis*). The second, published by Alves et al. [100], showed the antibiofilm, antimicrobial, and antiparasitic potential of *E. hyemale* extract against several infectious agents (bacteria, fungi, *Mycobacterium*, and *Trypanosoma*).

All the pharmacological activities described here can benefit in parallel the therapeutic management of kidney disorders. The anti-inflammatory activity related to some species could mitigate the damage caused by the high blood pressure levels suffered by the kidneys during systemic arterial hypertension or even the damage caused by diabetes. Accordingly, some species have also demonstrated significant antidiabetic actions. In addition, regarding the antimicrobial actions described by some species, these could have a significantly useful application against genitourinary infections, which could also benefit kidney damage. The multiple therapeutic possibilities for plants of the *Equisetum* genus are evident; however, many studies are needed to evaluate both the pharmacological potential and the safety concerning the use of the preparations. Finally, Table 3 summarizes the main scientific findings that demonstrate the therapeutic effects of different species of *Equisetum* in kidney disorders and other biological activities.

### 6. Final Considerations

This review reveals that the most widespread traditional use of *Equisetum* is as diuretic, followed by the treatment of genitourinary diseases. The most popular species from the *Equisetum* genus with medicinal use is *E. arvense*. Other species also demonstrate beneficial effects in experimental assays for different pharmacological purposes. However, few *in vivo* toxicity studies were conducted so far for most species, so there is no consensus on effective and toxic dosage. Hence, many species need to be explored in detail for scientific validation of popular use to induce diuresis and treat kidney and other associated diseases.

### Conflicts of Interest

The authors declare that they have no conflicts of interest.

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Supplementary Materials

Figure S1: chemical structure of the compounds identified in the *Equisetum* genus. Chemical structures are presented followed by their names, molecular weights, and references. (Supplementary Materials)

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