Tragia L. Genus: Ethnopharmacological Use, Phytochemical Composition and Biological Activity

Rodrigo Duarte-Casar 1,2 and Juan Carlos Romero-Benavides 2,*

Abstract: Tragia L. is a genus of plants belonging to the Euphorbiaceae family with worldwide intertropical distribution, composed of more than 150 species. In this literature review, 26 species of the genus used as medicinal plants were found, mainly in East Africa and the Indian subcontinent, with a variety of uses among which antibacterial, anti-inflammatory, anticancer and reproductive health are most common. Research has been done on a few of the species, mostly those of the Old World, with emphasis on four of them: Tragia involucrata Linn., Tragia spathulata Benth., Tragia benthamii Baker and Tragia plukenetii Radcl.-Sm., confirming several ethnomedicinal claims. Moreover, a variety of active phytochemicals have been isolated, mainly ethers, hydrocarbons, flavonoids and sterols. There is ample field for the evaluation of the activity of Tragia extracts and essential oils and the identification of their active compounds, particularly of the New World species, for which there is still very little research.

Keywords: Tragia; ethnopharmacology; phytochemicals; Euphorbiaceae; biological activities

1. Introduction

Plants have been used as a source of medicinal substances for a long time, with a use that amply predates history and presumably even mankind [1–3], and the discovery of active species and their use has historically been characterized by a trial-and-error approach [4]. This empirical knowledge has been and is being validated by systematic research and is used as a guideline to direct the search for better and new drugs, integrating ancestral knowledge and modern methods [5].

Among the plant families considered medicinal, Euphorbiaceae is well regarded. The ample geographical distribution of the family and the variety of stress conditions the plants grow in, which trigger the production of secondary metabolites [6], partially explain the abundance and variety of biologically active compounds found in the family and thus its medicinal activity [7,8].

This review endeavors to summarize the current knowledge about species of the Tragia genus, which belongs to the Euphorbiaceae family, concerning their medicinal properties, phytochemical basis, and in vitro and in vivo evidence and envisioning future research prospects.

2. Genus

The genus Tragia is one of the 317 genera in the Euphorbiaceae family. There are 161 accepted names belonging to 154 species in the Tragia genus, with “pantropical and warm temperate distribution” [9,10]. The etymology for the name of this genus comes from the Greek tragos, meaning goat. This name may stem either from the name of the German botanist Hieronymus Bock—Bock means “ram” or “he-goat” in German, or from the hairy appearance of the plant that would resemble a male goat [11].
Tragia species exhibit very ample morphological characters: they are perennial plants with herb, shrub, subshrub and twining vine growth habits, with lanceolate leaves presenting either entire or serrated margins. Plants belonging to this genus sting when touched due to the presence of leaf hairs with a needle-shaped crystal of calcium oxalate (raphide) in the terminal cells that is expelled on contact and punctures the skin, allowing irritants to enter and cause transient stinging [12,13], presumably a defense mechanism against herbivores [14]. Several common names for Tragias, such as noseburn (Tragia spp.), Indian stinging nettle (T. involucrata), fireman (T. volubilis) or stinging nettle creeper (T. durbanensis), are due to this stinging property. Figure 1 shows T. involucrata leaf hairs with raphides visible, taken in Kerala, India, and T. ramosa with clearly visible raphides, taken in Nevada, USA.

Species belonging to Euphorbiaceae in general and to Tragia in particular are still not fully settled [8], as new species are being discovered [15] and species are being reassigned to other genera [9,16], so the number of species in the genus is still subject to change.

3. Distribution and Localization

Species belonging to the Tragia genus are present in subtropical America, Eastern and Southern Africa, the Indian subcontinent and Northeastern Australia. Of the 154 species listed in the genus [17], 94 are found in Africa, 48 in America, 10 in Asia and 3 in Oceania, with some species such as T. arabica and T. plukenetii present both in Africa and Asia. The map in Figure 2 shows the intertropical distribution of Tragia species by country.

![Figure 1. Tragia involucrata leaves, left. Tragia ramosa showing leaf and stem, covered by long, rough leaf hairs. Scheme 3.0 license; right, Stan Shebs, GDFL license.](image1.png)

![Figure 2. Worldwide Tragia species distribution, by country.](image2.png)
4. Methodology

Published works (articles and patents) were searched on scientific databases—Science Direct, Google Scholar and Scopus—for each species of the genus, using inverted commas for an exact match, e.g., “Tragia acalyphoides”. Relevant articles were selected after removing search terms unrelated to the area of interest such as corrosion, reforestation or hare diet. When abundant results were obtained, the search was refined with more specific terms, for example “Tragia involucrata medicinal” or “Tragia involucrata ethnopharmacology”. Duplicate articles were removed, and the remaining articles were reviewed with a focus on ethnopharmacological uses, phytochemical composition and biological activity, both in vitro and in vivo. When possible, the latest articles, no older than 10 years, have been cited. Preprints were not included.

The research interest in \textit{Tragia} species in medical and health sciences has increased during the last twenty years. Figure 3 shows the number of publications that include the word Tragia in their text in the fields mentioned. Even though the subject is not a very popular one, a steady increase in appearances can be seen, with a marked increase between 2019 and 2020 and the first half of 2021.

![Figure 3. Publications containing the word Tragia since the year 2000 in Medical and Health sciences and in Chemical sciences. Data source: [18].](image)

Compared to the other genera in the \textit{Plukenietiae} tribe, \textit{Tragia} concentrates 67% of the research, compared to 12% for \textit{Cnesmone}, 10% for \textit{Acidoton}, 4% for \textit{Sphaerostylis} and 1% each for \textit{Megistostigma}, \textit{Pachystylidium}, \textit{Platygyna} and \textit{Tragiella} [18].

5. Ethnopharmacological Usage

Of the more than 150 species of the genus, few appear in the scientific literature, and even fewer are mentioned from an ethnopharmacological perspective. Notwithstanding, \textit{Tragia} species are a part of traditional medicinal systems of East Africa and the Indian subcontinent, such as Siddha and Ayurveda [19], with documented uses of \textit{T. involucrata} appearing as early as the 1st century CE [20] and with only a handful of mentions of \textit{Tragia} species in the New World pharmacopoeia, concerning mostly topical applications. There is concern over an excessive use of \textit{Tragia} species, e.g., \textit{Tragia bicolor}, which poses a conservation hazard [21,22].
Most of the interest in this genus has been focused on four species: *Tragia involucrata*, *Tragia spathulata*, *Tragia plukenetii* and *Tragia benthamii* [23], with the bulk of the research focused on *T. involucrata*. Nevertheless, several more species and their medicinal uses appear in literature. Table 1 summarizes the species with reported medicinal use along with their stated ethnopharmacological uses, when available. The Anatomical Therapeutic Chemical (ATC) Classification by the World Health Organization (WHO) is used to classify the uses for each species [24]. Figure 4 shows the geographical distribution of the documented uses. The ethnomedical uses of *Tragia* spp are most abundant in the Indian subcontinent and East and Southern Africa.

Table 1. *Tragia* species and their ethnopharmacological use. Species are listed in alphabetical order and validated against [25].

| Species                | Region                  | Plant Organs Used          | Use                           | Form of Usage | ATC Category | References |
|------------------------|-------------------------|----------------------------|-------------------------------|---------------|--------------|------------|
| *Tragia aliena* Pax and K.Hoffm. | Brazil                  | NS                         | Medicinal (not specified)    | NS            | V            | [26]       |
| *Tragia benthamii* Baker | Nigeria, Cameroon        | Whole plant, Leaves, roots | Abortifacient, Antimalarial   | Decoction     | LS           | [27]       |
| *Tragia bicolor* Miq.   | India, Sri Lanka         | NS                         | Medicinal                    | NS            | V            | [21]       |
| *Tragia brevipes* Pax.  | Rwanda, Kenya            | Leaves                     | Anticancer, Antgonorrhoenic   | Decoction     | L            | [29]       |
| *Tragia cinea* Bojer    | Ethiopia                 | Leaves                     | NS                            | G             |               | [33]       |
| *Tragia cordata* Michx. | America, Ethiopia        | Roots                      | Urinary tract and external parasites | Decoction     | G             | [39]       |
| *Tragia dixica* Sond.   | South Africa             | Leaves                     | Fatigue                       | NS            | V            | [40]       |
| *Tragia doryodes* M.G. Gilbert | Ethiopia            | Leaves, Stems              | Anthrax                       | Decoction     | J             | [41]       |
| *Tragia durbanensis* Kuntze. | South Africa           | NS                         | Skin rashes                   | NS            | D            | [42]       |
| *Tragia furialis* Bojer | Tanzania, Madagascar    | Roots                      | Abscess, Antimalarial         | Cold water maceration, drunk | J             | [43]       |
| *Tragia geraniifolia* Klotzsch ex Mull.Arg. | Argentina | Roots | Emollient                    | NS            | D            | [46]       |
| *Tragia gracils* Griseb. | Cuba                    | NS                         | Not specified                 | NS            | V            | [48]       |
| *Tragia hildebrandtii* Mull.Arg. | India              | NS                         | Not specified                 | NS            | V            | [49]       |
| *Tragia hispida* Wild.  | Sri Lanka                | NS                         | Tooth decay                   | NS            | A            | [50]       |
| *Tragia insuavis* Prain.| Kenya                   | Endophytes                 | Antibacterial                 | NS            | J            | [51]       |
| *Tragia involucrata* L. | Southern Asia           | Whole plant, Leaves, Roots | Analgesic, Antidiabetic, Anti-inflammatory | Decoction       | N            | [20,52]    |
| *Tragia meyeriana* Mull.Arg. | South Africa          | NS                         | Aphrodisiac, Antineoplastic | Decoction     | G             | [59]       |
| Species                      | Region                  | Plant Organs Used | Use                        | Form of Usage                                      | ATC Category | References |
|------------------------------|-------------------------|-------------------|----------------------------|----------------------------------------------------|--------------|------------|
| *Tragia mitis* Hochst. ex A. Rich. | Ethiopia               | Root              | Antidiarrheal              | Crushed, mixed with water and sugar                | A            | [62]       |
| *Tragia mixta* M.G.Gilbert    | Djibouti                | Leaves            | Analgesic                  | Heated Poultice                                    | N A          | [63] [64]  |
| *Tragia okamuny Pax*           | Namibia                 | Root              | Dizziness                  | Powdered, drunk with water                        | N V B G      | [65] [66]  |
| *Tragia plukertii* Radcl.-Sm.  | East Africa, India      | Leaves            | Antihyperglycemic          | Decoction                                          | A L          | [23]       |
| *Tragia praetervisa* Chakrab. & N.P. Balakr. | India, Sri Lanka | NS                | Not specified              | NS                                                  | V            | [49]       |
| *Tragia preussii* Pax          | Central African Republic | Leaves            | Rheumatism                 | NS                                                  | M            | [67]       |
| *Tragia pungens* (Forsk.) Mull.Arg. | Yemen                 | Whole plant       | Allergy and skin diseases  | Paste                                              | D M L G      | [68] [69] [70] |
| *Tragia ramosa* Torr.          | U.S.A., Mexico          | Leaves            | Not specified              | NS                                                  | V            | [71]       |
| *Tragia senegalensis* Mull. Arg | South Africa            | Whole plant       | Medicine (not specified)   | NS                                                  | V V          | [72] [73] |
| *Tragia sendleri* Prain        | Swaziland               | Leaves            | Azoospermia                | NS                                                  | G            | [74]       |
| *Tragia spathulata* Benth.     | West Africa             | Leaves            | Antibacterial              | NS                                                  | J            | [23] [76] |
| *Tragia subrenalis* Pax        | Uganda                  | Root              | Tuberculosis               | NS                                                  | J            | [77]       |
| *Tragia uberabana* Mull. Arg.  | Brazil                  | NS                | Medicinal Toxic            | NS                                                  | V V          | [78]       |
| *Tragia yegeli* Keay           | Burkina Faso            | Whole plant       | Abortifacient              | Decoction                                          | G            | [79]       |
| *Tragia zohelis* L.            | Mexico, Antilles, Brazil| Leaves, Stem, Root| Diuretic                   | Decoction                                          | G V G        | [80] [26] [46,81] |
| *Tragia yucatanensis* Millisp.| Belize, Guatemala, Mexico| Leaves            | Burns                      | Rheumatism                                         | Topical D M  | [82]       |

NS: not specified. ATC categories are as follows: A: alimentary tract and metabolism, B: blood and blood-forming organs, C: cardiovascular system, D: dermatological, G: genitourinary system and sex hormones, H: systemic hormonal preparations, excluding sex hormones and insulins, J: anti-infective for systemic use, L: antineoplastic and immunomodulating agents, M: musculo-skeletal system, N: nervous system, P: antiparasitic products, insecticides and repellents; R: respiratory system, S: sensory organs; V: various [24], not present in the classification. STDs: sexually transmitted diseases.

According to the ATC classification, the most frequent ethnopharmacological uses of *Tragia* spp. in ethnopharmacology are: genitourinary system and sex hormones, with 19% of occurrences (15 of 77); nervous system, with 12%; and alimentary tract and metabolism, anti-infective for systemic use and antineoplastic and immunomodulating agents with 10% of occurrences each. The “various” classification presents 17% of occurrences, which include non-specified and vague uses, such as “toxic” or “medicinal”.

As for the morphological structures used per species, the most common are the leaves, 38%; followed by “not specified”, 33%; whole plant, 15%; roots, 13% and a single occurrence of endophytes (3%).
6. Biological Activity

Biological activity tests of *Tragia*, both in vitro and in vivo, are performed mostly with plant extracts and to a much lesser degree with essential oils: leaf, root or the whole plant, although ethnopharmacological uses mostly employ the plant via infusions, decoctions or ashes [23,35]. Different solvents and solvent mixtures have been used for the extracts, mainly methanol and ethanol. Due to the presence of *Tragia* in ethnomedical traditions in Africa and Asia, there is a team of research about the bioactivity of Old World *Tragia* extracts that have confirmed their activity and potency in some cases. Not all the health claims or traditional uses recorded have been validated through research. Again, the bulk of the research is centered on *T. involucrata*.

6.1. In Vitro Activity

Extracts of *T. benthamii*, *T. brevipes*, *T. involucrata*, *T. pungens* and *T. spatulatha* have been tested to ascertain their in vitro activity for a variety of uses. The in vitro research is summarized in Figure 5.

Cases in which the efficacy has been shown in vitro are listed in Table 2.
Table 2. In vitro activity of *Tragia* extracts. Species are in alphabetical order.

| Species       | Extract               | Plant Organs Used | Biological Activity   | Biological Model                           | Effect                                    | Methodology                              | Reference |
|---------------|-----------------------|-------------------|-----------------------|--------------------------------------------|-------------------------------------------|------------------------------------------|-----------|
| *T. benthamii*| Methanol              | Whole plant       | Antibacterial         | 28 strains (sensitive and MDR) of *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, *Enterobacter aerogenes*, *Escherichia coli*, *Providencia stuartii* | Effective against 11/28 strains (39.3%) | INT colorimetric assay [83]              |           |
| *T. brevipes* | Methanol: water 9:1   | Leaf              | Antibacterial         | *Enterobacter aerogenes*, *Bacillus cereus*, *Serratia liquefaciens*, *Proteus vulgaris* | Inhibition zones (mm)                     | 500 mg/mL extract—well diffusion assay [84] |           |
| *T. brevipes* | Methanol:DCM 1:1      | Leaf              | Antiproliferative     | DU145 +IC₅₀: 30 µg/mL Extract              |                                           | MTT                                       | [85]      |
| *T. involucrata* | Chloroform           | Root              | Antidiabetic          | Fertile eggs of white leghorn chicken +    |                                           | 0.5, 1 mg/egg, Streptozotocin-induced diabetes [86] |           |
| *T. involucrata* | Ethyl acetate        | Root              | Antibacterial, Antifungal | Staphylococcus aureus, Bacillus subtilis, Bacillus brevis, Staphylococcus epidermidis, Escherichia coli, Shigella disenteriae, Pseudomonas aeruginosa, Vibrio cholera | Inhibition zones (mm)                     | 50–250 mg/mL, Disc diffusion [53] |           |
| *T. involucrata* | Isolated hydrocarbons and ethers | Leaf | Antifungal | Rhizopus stolonifer, Aspergillus niger, Alternaria solani, Macer indicus, Chaetomium globosum, Tilletia indica | Inhibition zone mm | +16 ± 0.3 mm, +15 ± 0.6 mm, +10 ± 0.5 mm | Agar disc diffusion [87] |           |
| *T. involucrata* | Isolated hydrocarbons and ethers | - | Antibacterial | Burkholderia pseudomallei (TES21), Burkholderia pseudomallei (KHW), Klebsiella pneumoniae (ATCC15180), Pseudomonas aeruginosa (ATCC27853), Vibrio danoela, Salmonella typhi (ATCC351812) | Inhibition zone mm | +23, +25, +20, +19, +28 | Agar disc diffusion [88] |           |
| Species                  | Extracts                          | Plant Organs Used | Biological Activity | Biological Model | Effect                  | Methodology                          | Reference |
|-------------------------|-----------------------------------|-------------------|---------------------|------------------|-------------------------|--------------------------------------|-----------|
| *T. involucrata*        | Methanol                          | Leaf              | Antiproliferative   | K562 cell lines  | -                       | CHCl₃, AcOEt                         | [89]      |
|                         | Ethyl acetate                     |                   |                     |                  | -                       |                                     |           |
|                         | Chloroform                        |                   |                     |                  | -                       |                                     |           |
|                         | Petroleum ether                   |                   |                     |                  | -                       |                                     |           |
| *T. involucrata*        | Water +NP                         | Leaf              | Antiurolithiatic    |                  | +                      | Struvite crystal growth inhibitory effect | [80]      |
| *T. involucrata*        | Methanol                          | Whole plant       | Radioprotective     | Cultured human peripheral lymphocytes | +Pretreatment (10 μg mL⁻¹) | ⁶⁰Co gamma irradiation | [91]      |
| *T. meyeriana and other plant species* | Boiling water                     | Whole plant       | Immunomodulatory    | Isolated peripheral blood mononuclear cells | + | S. aureus stimulation. Inflammatory cytokine secretion in THP-1 monocytes | [61]      |
| *T. pungens*            | Methanol                          | NS                | Antibacterial       |                  | -                      | Staphylococcus aureus                | [69]      |
|                         |                                  |                   | Cytotoxic           |                  | -                      |                                      |           |
|                         | Bacillus subtilis                 |                   | -                   |                  |                        |                                      |           |
|                         | Micrococcus flavus                |                   | -                   |                  |                        |                                      |           |
|                         | Pseudomonas aeruginosa            |                   | -                   |                  |                        |                                      |           |
|                         | Candida maltosa                   |                   | -                   |                  |                        |                                      |           |
|                         | FL cells                          |                   | -                   |                  | +                      | Cytotoxicity. IC₅₀: 70 μg/mL          |           |
| *T. spatulatha*         | Ethanol                           | Leaf              | Antibacterial       |                  | +21                    | Staphylococcus aureus, Proteus mirabilis, Klebsiella pneumoniae, Salmonella typhi, Streptococcus pneumoniae, Escherichia coli, Candida albicans, Aspergillus flavus, Fusarium solani | [76]      |
|                         | Methanol                          |                   | Antifungal          |                  | +25                    |                                      |           |
|                         | Acetone                           |                   |                     |                  | +25                    |                                      |           |

MDR: multi-drug resistant. NP: nanoparticle. DCM: dichloromethane. NS: not specified; INT: p-Iodonitrotetrazolium chloride; MTT: 3-(4,5-dimethyl-2-thiazoly)-2,5-diphenyltetrazolium bromide; MIC: minimum inhibitory concentration; AcOEt: ethyl acetate; AgNP: silver nanoparticles; + active. - not active.
In vitro biological activity tests devote the most attention to leaves (36%), with whole plant and root used to a lesser extent, with both 14%. Extraction solvents are methanol (47%), DCM (5%), Ethyl acetate (10%), water (6%), chloroform (5%), petroleum ether (5%), ethanol (5%) and acetone (5%). This solvent usage supports the assumption that most active compounds are moderately polar and are thus extracted with polar solvents.

Testing centers on antibacterial (41%) and antifungal (18%) activity of the extracts, with antiproliferative (12%) and antidiabetic, antiarthritic, radioprotective, immunomodulatory and cytotoxic effects (6% each) behind. This is a different profile than what was found in the ethnomedicinal claims, which centers on the genitourinary system and sex hormones. This is justified because aphrodisiacs do not have the expected properties [92].

### 6.2. In Vivo Activity

Besides in vitro activity testing, research has been done in animal models, mostly mice and also chicks, with at least one clinical trial performed in humans. The *Tragia* extracts evaluated in vivo, summarized in Figure 6 and Table 3, are obtained from four species: *T. benthamii, T. furialis, T. involucrata* and *T. plukenetii*.

![Figure 6. Summary of in vivo activity of Tragia extracts.](image_url)

**Table 3. In vivo activity of Tragia extracts.**

| Species       | Extract          | Plant Organs Used | Animal Model       | Activity                 | Results                                                                 | Reference |
|---------------|------------------|-------------------|--------------------|--------------------------|-------------------------------------------------------------------------|-----------|
| *T. benthamii*| Ethanol          | Whole plant       | Swiss albino mice  | Antimalarial             | −Very poor activity against *P. berghei* (NK-65) at 50 mg·kg⁻¹ bw.       | [27]      |
| *T. benthamii*| Water            | NS                | Chick              | Anti-inflammatory        | +Carrageenan-induced foot edema. Maximal inhibition 84.3% at 300 mg/kg bw. | [93]      |
| *T. furialis* | Ethanol-water    | NS                | White albino mice  | Antimalarial             | +IC50: 639.3 mg·kg⁻¹ bw against *P. berghei*.                           | [43]      |
| *T. involucrata* | Benzene: Ethyl acetate 1:1 | Root | *Culex quinquefasciatus* | Larvicidal               | +0.1–0.4% te/v; Oviposition and phagostereference, larvicidal.          | [94]      |
| *T. involucrata* | Ethanol         | Leaf              | Albino rats (male) | Nephroprotective         | +250 and 500 mg/kg bw. Decrease in serum urea and creatinine in acetaminophen-induced toxicity. | [95]      |
| *T. involucrata* | Hexane Ethyl acetate | Aerial parts | Swiss albino mice | Antitumor                | +50–150 mg/kg bw. Ehrlich’s Ascites Carcinoma. DD antitumor activity and increased life span for both extracts. | [96]      |
| *T. involucrata* | Hot water        | NS                | Wistar rats (male) | Diuretic                 | +1650, 2200 mg/kg bw. Loop diuretic action.                             | [56]      |
| *T. involucrata* | Hot water—freeze dried | Whole plant      | Clinical trial     | Antidiabetic             | 240 mL·decouction/day; FPG decrease from 164.4 ± 20.4 to 130.9 ± 16.2 mg/dL. | [52]      |
| *T. involucrata* | Methanol         | Leaf              | Swiss albino mice  | Analgesic, Anxiolytic    | +200, 400 mg/kg bw. Acetic acid writhing and formalin-induced paw licking; behavioral tests; pentobarbital-induced sleep time. | [97]      |
### Table 3. Cont.

| Species        | Extract | Plant Organs Used | Animal Model     | Activity                  | Results                                                                 | Reference |
|----------------|---------|-------------------|------------------|---------------------------|-------------------------------------------------------------------------|-----------|
| *T. involucrata* | Methanol | Leaf              | Wistar rats      | Antibacterial             | +100, 200 mg/kg bw. Wound healing in *S. aureus* infections.             | [98]      |
| *T. involucrata* | Methanol | Leaf              | Swiss albino mice| Antiepileptic             | +400, 800 mg/kg bw. MES, PTZ induced convulsions. DD                   | [99]      |
| *T. involucrata* | Methanol | NS                | Swiss albino mice| Radioprotective           | +100 mg/kg bw. DD survival increase                                      | [100]     |
| *T. involucrata* | Methanol | Root              | Charles-Foster rats Swiss albino mice | Analgesic Anti-inflammatory | +Carrageenan paw edema, cotton pellet granuloma, acetic acid writhing. | [101]     |
| *T. involucrata* | Methanol | Root              | Wistar rats      | Antibacterial             | +100, 200 mg/kg bw. Wound healing in *S. aureus* infections             | [102]     |
| *T. involucrata* | Methanol | Root              | Charles—Foster rats Swiss albino mice | CNS depressant            | +100–300 mg/kg bw. Behavioral pattern, spontaneous motility, pentobarbital-induced sleep, body temperature, aggressive behavior pattern and conditioned avoidance response (CAR). | [103]     |
| *T. involucrata* | Methanol Chloroform | Whole plant | Albino rats | Anti-inflammatory | +100, 300 mg/kg bw. Both extracts. Carrageenan paw oedema.             | [54]      |
| *T. involucrata* | Methanol Ethyl acetate | Whole plant | Swiss albino mice | Analgesic | +500 mg/kg bw. Acetic acid model; tail flick model analgesic activity. | [55]      |
| *T. involucrata* | Water | Leaf              | Wistar rats Swiss mice (male) | Anti-inflammatory | +50–400 mg/kg bw. in carrageenan-induced hindpaw edema and cotton pellet granuloma models. | [104]     |
| *T. involucrata* | Water | Leaf              | Wistar rats Swiss mice (male) | Antiulithiatic            | +200 mg/kg bw. CaOx stone formation inhibition in ethylene glycol-induced urolithiasis. | [90]      |
| *T. plukenetii* | Ethanol | Aerial parts      | Wistar rats Swiss mice (male) | Antihyperglycemic         | +At oral dose of 150 and 300 mg/kg bw. Oral glucose tolerance test in alloxan induced diabetic rats. | [105]     |
| *T. plukenetii* | Ethanol | Whole plant       | Wistar rats Guinea pigs | Antipyretic              | +100 mg/kg bw. +Antipyretic: Brewer’s yeast-induced hyperpyrexia method. | [106]     |
| *T. plukenetii* | Ethanol | Whole plant       | Swiss albino mice (male) | Antidiuretic Antiasthmatic Antalgic Antispasmodic | +Diuretic: in vivo Lipschitz test method. +Antiansthamatic: Isolation of guinea pig ileum preparation; histamine-induced bronchocnstruction. +Analgesic: acetic acid writhing response. +Antispasmodic: studies on isolated rabbit jejunum. | [106]     |
| *T. plukenetii* | Ethanol | Whole plant       | Swiss albino mice (male) | Antitumor                | +100–300mg/kg bw. Ehrlich ascites carcinoma survivability. Antioxidant parameters increased DD. | [107]     |
| *T. plukenetii* | Methanol Benzene Chloroform | Leaf | Swiss albino mice (male) | Anticonvulsant           | +100 mg/kg bw. Methanol extract against PTZ-induced convulsions.         | [108]     |

NS: not specified; −: no activity; +: activity present; DD: dose-dependent, bw: body weight; MES: maximal electroshock; PTZ: pentylenetrazol; PTX: picrotoxin; FPG: fasting plasma glucose; SGOT: serum glutamic oxaloacetic transaminase; SGPT: serum glutamic pyruvic transaminase; ALP: alkaline phosphatase.

Most of the research (73%) centers on *T. involucrata*, with *T. plukenetii* (18%), *T. benthamii* (9%) and *T. furialis* (5%) behind. In vivo assay extracts were obtained from leaves (29%), whole plant (25%), root (21%) and aerial parts (8%). Solvents used are methanol (48%), ethanol (26%) and water (13%), which shows that most active compounds are polar and are thus extracted with polar solvents.

For both in vitro and in vivo testing, the most common effect is antibacterial and antimicrobial with 22% of the reviewed studies. This is higher than the 10% reported in the ethnopharmacological uses. Effects having to do with cancer prevention and treatment—antiproliferative, antitumor, cytotoxic immunomodulatory and radioprotective—add up to 17% of the reported effects, which makes it the second most frequent use. Analgesic and anti-inflammatory activity is equally reported in 10% of the tests.
The findings reported in literature validate several medicinal use cases for *Tragia* species and dismiss some claims, e.g., *T. meyeriana* as an antineoplastic [60].

7. Phytochemical Composition

Phytochemical studies allow for the identification, separation and isolation of compounds of interest [109]. Based on phytochemical screenings published in the literature, the main secondary metabolites found in *Tragia* species extracts are alkaloids, glycosides, flavonoids, and sterols [23,110].

Some compounds found in plants belonging to the *Tragia* genus, classified according to their chemical nature, are listed in Table 4. Where applicable, the biological activity of the identified compound has been mentioned.

Identification of the compounds relies heavily on spectroscopic and spectrometric methods [109], and chromatography retention times and comparison with the literature are also used for tentative identification.

Figure 7 shows the structure of some of the compounds identified in *Tragia* extracts and oils, mentioning their biological activity in bold when reported. As expected in plant extracts, there is a variety of secondary metabolites in the form of terpenoids and flavonoids. Ethers and non-terpenoid hydrocarbons are reported as having antibacterial activity, and they are not in any of the common groups of secondary metabolites. There is more information about the activity of the extracts and essential oils than about the activity of compounds on their own. The recent discovery of anti-inflammatory peptides in *Tragia benthamii* extracts [93] opens a new area of interest in the research of *Tragia* species.

A strength of the genus is its diversity and its pantropical distribution, which makes it readily available in most tropical countries. A weakness would be that, despite the interest shown concerning *T. involucrata* and other traditionally medicinal species, there appear to be no drugs derived from plants of these species, remaining in the realm of herbal remedies and plant extracts, entailing less medicinal interest than other genera of the *Euphorbiaceae* family, notably *Euphorbia* [8]. This can be attributed to the stage of research, with most work performed in vitro or in vivo and with a single clinical trial [52]. Hopefully the current research will advance into new drugs.
| No. | Compound                                                                 | Methodology Used                                      | Species          | Collection area | Plant Organ Used | Use                  | Effect                          | Reference |
|-----|--------------------------------------------------------------------------|------------------------------------------------------|------------------|----------------|------------------|----------------------|---------------------------------|-----------|
| 1   | 1,1-diethoxy-2-methylpropane                                             | Ethanol extract GC, MS                               | T. plukenetii    | NS             | Whole plant      | NS                   | Aldehydes                       | [111]     |
| 2   | 16-heptadecenal                                                          | Ethanol extract GC, MS                               | T. plukenetii    | NS             | Whole plant      | NS                   | NS                              | [111]     |
| 3   | Hexanal                                                                  | Hydrodistillation GC/GC-MS                            | T. benthamii     | Ibadan, Nigeria | Leaves           | NS                   | NS                              | [112]     |
| 4   | (E)-4-(1-hydroxypropyl)-7,8-dimethyl-9-(prop-1-en-1-yl)-[1,3] dioxolo   | Acidified ethanol extract GC, MS, LC                 | T. plukenetii    | NS             | Whole plant      | NS                   | NS                              | [111]     |
| 5   | 4-oxo-4H-pyran-2,6-dicarboxylic acid bis-[6-methyl-heptyl] ester         | Ethanol extract IR                                   | T. involucrata   | Salem, India   | Roots            | Antidiabetic          | Blood glucose reduction         | [86]      |
| 6   | Ethyl linoleate                                                          | Ethanol extract GC, MS                               | T. plukenetii    | NS             | Whole plant      | NS                   | NS                              | [111]     |
| 7   | Ethyl palmitate                                                          | Ethanol extract GC, MS                               | T. plukenetii    | NS             | Whole plant      | NS                   | NS                              | [111]     |
| 8   | Vinyl hexyl ether                                                        | Aqueous extract GC, MS                               | T. involucrata   | Tamil Nadu, India | Leaf               | Antibacterial          Escherichia coli Proteus vulgaris Staphylococcus aureus | MBC 12.25 µg/mL | [98,113] |
| 9   | 3-(2,4-dimethoxyphenyl)-6,7-dimethoxy-2,3-dihydrochromen-4-one           | Ethyl acetate extract FTIR, MS, $^1$H NMR           | T. involucrata   | Odisha, India  | Root             | Antibacterial         | MIC 1.25-12.5 µg/mL             | [53]      |
| 10  | Iridin                                                                   | Ethyl acetate extract FTIR, MS, $^1$H NMR           | T. involucrata   | Odisha, India  | Root             | Toxic                |                                 | [53]      |
| 11  | Quercetin                                                                | Ethyl acetate extract FTIR, MS, $^1$H NMR           | T. involucrata   | Odisha, India  | Root             | Antioxidant           |                                 | [53]      |
| 12  | Rutin                                                                    | Ethyl acetate extract FTIR, MS, $^1$H NMR           | T. involucrata   | Odisha, India  | Root             | Antioxidant           |                                 | [53]      |
| 13  | 2,5-dithia-3,6-diazabicyclo[2.2.1]heptane                                | 95% aqueous ethanol extraction $^1$H, $^{13}$C NMR  | T. benthamii     | Ibadan, Nigeria | Whole plant      | NS                   |                                 | [114]     |

Table 4. Compounds isolated/identified in *Tragia* extracts and oils and their biological effect.
| No. | Compound Identified Isolated Methodology Used | Species Collection area | Plant Organ Used | Use | Effect | Reference |
|-----|---------------------------------------------|-------------------------|-----------------|-----|--------|-----------|
|     | Hydrocarbons                                |                         |                 |     |        |           |
| 14  | 2,6-dimethylheptane X Aqueous extract GC, MS | *T. involucrata* Tamil Nadu, India Leaf Antibacterial *Proteus vulgaris* MBC 10 µg/mL [98] |
| 15  | 2,4-dimethylhexane X Aqueous extract GC, MS | *T. involucrata* Tamil Nadu, India Leaf Antibacterial *Staphylococcus aureus* MBC 12.25 µg/mL [98] |
| 16  | 2-methylnonane X Aqueous extract GC, MS     | *T. involucrata* Tamil Nadu, India Leaf Antibacterial *Escherichia coli* MIC 5.0 µg/mL [98] |
| 17  | Shellsol (2-methyldecane) X Aqueous extract GC, MS | *T. involucrata* Tamil Nadu, India Leaf Antibacterial *Proteus vulgaris* MBC 25.0 µg/mL [98] |
| 18  | 3,5-di-tert-butyl-4-hydroxyanisole X 95% aqueous ethanol extraction 1H, 13C NMR | *T. benthamii* Ibadan, Nigeria Whole plant Antioxidant Muscle relaxant, bronchodilating and anti-allergic effects [114] |
| 19  | 5-hydroxy-1-methylpiperdin-2-one X Methanol extract IR, 1H, 13C RMN, LC | *T. involucrata* Kerala, India Leaf Antihistamine | |
|     | Polyols                                      |                         |                 |     |        |           |
| 20  | Erythritol X 95% aqueous ethanol extraction 1H, 13C NMR | *T. benthamii* Ibadan, Nigeria Whole plant NS NS [114] |
| 21  | Glycerol X 95% aqueous ethanol extraction 1H, 13C NMR | *T. benthamii* Ibadan, Nigeria Whole plant NS NS [114] |
|     | Terpenoids                                   |                         |                 |     |        |           |
| 22  | 10,13-dimethoxy-17-(6-methylheptan-2-yl)-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[α]phenanthrene. X Ethyl acetate extract FTIR, MS, 1H NMR | *T. involucrata* Odisha, India Root NS NS [53] |
| 23  | Stigmasterol X Aqueous extract GC, MS        | *T. involucrata* Ibadan, Nigeria Leaf NS NS [98] |
| 24  | Caryophyllene X Ethanol extract GC/GC-MS     | *T. benthamii* Ibadan, Nigeria Leaves Anti inflammatory [112] |
| 25  | Citronellal X Ethanol extract IR, 1H RMN, LC | *T. ramosa* Maharashtra, India Leaves Antibacterial [71] |
| 26  | Clerodane X Ethanol extract GC/GC-MS         | *T. ramosa* Maharashtra, India Leaves NS NS [71] |
| 27  | Geranylacetone X Ethanol extract GC/GC-MS    | *T. benthamii* Ibadan, Nigeria Leaves NS NS [112] |
| No. | Compound Identified | Isolated | Methodology Used | Species | Collection area | Plant Organ Used | Use | Effect | Reference |
|-----|---------------------|----------|------------------|---------|----------------|------------------|-----|--------|-----------|
| 28  | Neophytadiene (2-(4,8,12-Trimethyltridecyl)buta-1,3-diene) | X | X | Ethanol extract GC, MS | *T. plukenetii* | NS | Whole plant | NS | NS | [111] |
| 29  | Phytol | X | X | 95% aqueous ethanol extraction 1H, 13C NMR | *T. benthamii* | Ibadan, Nigeria | Whole plant | NS | NS | [114] |
| 30  | Squalene (all trans) | X | X | Ethanol extract GC, MS | *T. plukenetii* | NS | Whole plant | NS | NS | [111] |
| 31  | α-terpinene | X | X | Ethanol extract IR, 1H RMN, LC | *T. ramosa* | Maharashtra, India | Leaves | Antiinflammatory, Antimicrobial | NS | [71] |

GC: gas chromatography; MS: mass spectrometry; LC: liquid chromatography; IR: infrared spectroscopy; NMR: nuclear magnetic resonance; FTIR: Fourier transform infrared spectroscopy; Q-TOF: quadrupole time of flight mass spectrometry; TLC: thin layer chromatography; NS: not specified.
Identification of the compounds relies heavily on spectroscopic and spectrometric methods [109], and chromatography retention times and comparison with the literature are also used for tentative identification.

Figure 7 shows the structure of some of the compounds identified in Tragia extracts and oils, mentioning their biological activity in bold when reported. As expected in plant extracts, there is a variety of secondary metabolites in the form of terpenoids and flavonoids. Ethers and non-terpenoid hydrocarbons are reported as having antibacterial activity, and they are not in any of the common groups of secondary metabolites. There is more information about the activity of the extracts and essential oils than about the activity of compounds on their own. The recent discovery of anti-inflammatory peptides in Tragia benthamii extracts [93] opens a new area of interest in the research of Tragia species.

Figure 7. Compounds identified in Tragia extracts and oils.

8. Conclusions

Species belonging to the Tragia genus are present in traditional medicine in several cultures and have multiple uses, among which antibacterial, anticancer and aphrodisiac are most frequent. There is scientific evidence that supports the use of these species in medicine, both at the extract level and at the active compound level, with in vivo tests in
rats and mice, but there are no drugs derived from the species yet. The activity reported most frequently for *Tragia* extracts is antimicrobial and cancer-related, which suggests further research in those areas.

Less than 20% of the *Tragia* species are considered medicinal. This implies vast potential for screening and discovery of active compounds.

Most ethnopharmacological reports come from Asia and Africa, mainly East Africa and the Indian subcontinent. New world *Tragia* species have not been sufficiently studied and may prove to be a rich source of extracts and phytochemicals for drug research. Future directions for research include nanoparticles, the research into peptides extracted from *Tragia* species and the validation of medicines containing *Tragia* extracts against SARS-CoV-2.

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**References**

1. Solecki, R.S. Shanidar IV, a Neanderthal Flower Burial in Northern Iraq. *Science* 1975, 190, 880–881. [CrossRef]
2. Ur Rehman, F.; Kalsoom, M.; Adnan, M.; Fazeli-Nasab, B.; Naz, N.; Ilahi, H.; Ali, M.F.; Ilyas, M.A.; Yousaf, G.; Toor, M.D.; et al. Importance of Medicinal Plants in Human and Plant Pathology: A Review. *Int. J. Pharm. Biomed. Res.* 2021, 8, 1–11. [CrossRef]
3. Marrelli, M. Medicinal Plants. *Plants* 2021, 10, 1355. [CrossRef]
4. Jamshidi-Kia, F.; Lorigooini, Z.; Amini-Khoei, H. Medicinal Plants: Past History and Future Perspective. *J. Herbmed Pharmacol.* 2018, 7, 1–7. [CrossRef]
5. Katiyar, C.; Kanjilal, S.; Gupta, A.; Katiyar, S. Drug Discovery from Plant Sources: An Integrated Approach. *AYU Int. Q. J. Res. Ayurveda* 2012, 33, 10–19. [CrossRef]
6. Li, Y.; Kong, D.; Fu, Y.; Sussman, M.R.; Wu, H. The Effect of Developmental and Environmental Factors on Secondary Metabolites in Medicinal Plants. *Plant Physiol. Biochem.* 2020, 148, 80–89. [CrossRef]
7. Coy Barrera, C.A.; Gómez, D.C.; Castiblanco, F.A. Importancia Medicinal Del Género Croton (Euphorbiaceae). *Rev. Cuba. Plantas Med.* 2016, 21, 234–247.
8. Mwine, J.T.; Damme, P.V. Why Do Euphorbiaceae Tick as Medicinal Plants? A Review of Euphorbiaceae Family and Its Medicinal Features. *J. Med. Plants Res.* 2011, 5, 652–662.
9. Gillespie, L.J.; Cardinal-McTeague, W.M.; Wurdack, K.J. Monadelpha (Euphorbiaceae, Plukenetieae), a New Genus of Tragiinae from the Amazon Rainforest of Venezuela and Brazil. *PhytoKeys* 2020, 169, 119–135. [CrossRef]
10. POWO Tragia Plum. Ex L. | Plants of the World Online | Kew Science. Available online: http://powo.science.kew.org/taxon/urn:lsid:ipni.org:names:327688-2 (accessed on 25 October 2021).
11. Urtecho, R. Tragia—FNA. Available online: http://dev.semanticfna.org/Tragia (accessed on 26 April 2021).
12. Naudé, T.W.; Naidoo, V. Oxalates-containing plants. In *Veterinary Toxicology*; Elsevier: Amsterdam, The Netherlands, 2007; pp. 880–891. ISBN 978-0-12-370467-2. [CrossRef]
13. Prasad, R.; Shivay, Y.S. Oxalic Acid/Oxalates in Plants: From Self-Defence to Phytoremediation. *Curr. Sci.* 2017, 112, 1665–1667. [CrossRef]
14. Ensikat, H.-J.; Wessely, H.; Engeser, M.; Weigend, M. Distribution, Ecology, Chemistry and Toxicology of Plant Stinging Hairs. *Toxins* 2021, 13, 141. [CrossRef]
15. Freire de Sá Cordeiro, W.P.; Athié-Souza, S.M.; Laurénio de Melo, A.; Ferreira de Sales, M. A New Endangered Species of Tragia (Euphorbiaceae) from the Brazilian Atlantic Forest. *Syst. Bot.* 2020, 45, 839–844. [CrossRef]
16. Freire de Sá Cordeiro, W.P.; Athié-Souza, S.M.; Buril, M.T.; de Melo, A.L.; de Sales, M.F. Chicomendes (Euphorbiaceae, Tragiinae): A New Amazonian Genus Segregated from Tragia. *Plant Syst. Evol.* 2021, 307, 46. [CrossRef]
17. Govaerts, R. *World Checklist and Bibliography of Euphorbiaceae (and Pandaceae)*; Royal Botanic Gardens: Kew, UK, 2000; Volume 1, ISBN 978-1-900347-83-9.
Plants 2021, 10, 2717

46. Barboza, G.E.; Cantero, J.J.; Núñez, C.; Arisa Espinar, L.; Pacciaroni, A. del V. Medicinal Plants: A General Review and a Phytochemical and Ethnopharmacological Screening of the Native Argentine Flora. *Kutziana* 2009, 34, 7–365.

47. Goleniowski, M.E.; Bongiovannino, G.A.; Palacio, L.; Núñez, C.O.; Cantero, J.J. Medicinal Plants from the “Sierra de Comechingones”, Argentina. *J. Ethnopharmacol.* 2006, 107, 324–341. [CrossRef]

48. Carlonmagno, A.; Pardini, A.; Contino Esquijerosa, Y. Medicinal Plants in Ethnobotanical and Religious Traditions in Cuba: A First Review and Updating. 2013. Available online: https://www.researchgate.net/profile/Anna-Carlomagno/publication/27686636_Medicinal_plants_in_ethnobotanical_and_religious_traditions_in_Cuba_a_first_review_and_updating/links/55b088a080eaaf3b9afea7/Medicinal-plants-in-ethnobotanical-and-religious-traditions-in-Cuba-a-first-review-and-updating.pdf (accessed on 15 April 2021).

49. Shiddamallayya, N.; Rao, R.; Doddamani, S.; Venkateshwaru, G. A Glimpse on Forest Flora and Indian System of Medicine Plants of Chitradurga District, Karnataka. *Int. J. Herb. Med.* 2016, 4, 25–33.

50. Hmhl, K.; Ngwnd, G. Medical Formulas for Krimidanta (Dental Caries) in Indigenous Medicine in Sri Lanka—A Literary Review. *Int. J. Ayurveda Pharma Res.* 2016, 4, 52–56.

51. Velma, W.N.; Isabel, N.W.; Meshack, A.O.; Josphat, C.M. Isolation, Identification and Bioactivity of Fungal Endophytes from Selected Kenyan Medicinal Plants. *Afr. J. Microbiol. Res.* 2018, 12, 405–412. [CrossRef]

52. Pallie, M.; Perera, P.; Goonasekara, C.; Kumarasinghe, N.; Arawwawala, M. Efficacy and Safety of Freeze-Dried Form of *Tragia involucrata* L. Decoction in Treating Diabetes: A Randomized Controlled Clinical Trial. *Clin. Trials Degener. Dis.* 2020, 5, 31–36. [CrossRef]

53. Panda, D.; Dash, S.K. Phytochemical Examination and Antimicrobial Activity of Various Solvent Extracts and the Selected Isolated Compounds from Roots of *Tragia involucrata* Linn. *Int. J. Pharm. Sci. Drug Res.* 2012, 4, 44–48.

54. Hosahally, R.V.; Seru, G.; Sutar, P.S.; Joshi, V.G.; Sutar, K.P.; Karigar, A.A. Phytochemical and Pharmacological Evaluation of Tragia Cannabina for Anti-Inflammatory Activity. *Int. Curr. Pharm. J.* 2012, 1, 213–216. [CrossRef]

55. Alimuzzaman, M.; Ahmed, M. Analgesic Activity of *Tragia involucrata*. *Dhaka Univ. J. Pharm. Sci.* 2007, 4, 35–38. [CrossRef]

56. Pallie, M.S.; Perera, P.K.; Goonasekara, C.L.; Kumarasinghe, K.M.N.; Arawwawala, L.D.A.M. Evaluation of Diuretic Effect of the Hot Water Extract of Standardized *Tragia involucrata* Linn., in Rats. *Int. J. Pharmacol.* 2018, 13, 83–90. [CrossRef]

57. Alanazi, A.; Anwar, M.J.; Ahmad, M.A. Hepatoprotective and Antioxidant Activity of *Tragia involucrata* Root Extracts against CCl4 Induced Hepatotoxicity in Rats. *Pharm. Lett.* 2015, 7, 146–152.

58. Edirweera, E.; Ratnasooriya, W. A Review on Herbs Used in Treatment of Diabetes Mellitus by Sri Lankan Ayurvedic and Traditional Physicians. *Ayu* 2009, 30, 373–391.

59. Drewes, S.E.; Selepe, M.A.; Van Heerden, F.R.; Archer, R.H.; Mitchell, D. Unravelling the Names, Origins and Chemistry of “Muthis” Used for Male Sexual Disorders in KwaZulu-Natal, South Africa. *S. Afr. J. Bot.* 2013, 88, 310–316. [CrossRef]

60. Charlson, A.J. Antineoplastic Constituents of Some Southern African Plants. *J. Ethnopharmacol.* 1980, 2, 323–335. [CrossRef]

61. Ngcobo, M.; Gqaleni, N.; Naidoo, V.; Cele, P. The Immune Effects of an African Traditional Energy Tonic in In Vitro and In Vivo Models. *Evid. Based Complement. Altern. Med.* 2017, 2017, 1–14. [CrossRef]

62. Yineger, H.; Yewhalaw, D.; Teketay, D. Ethnomedicinal Plant Knowledge and Practice of the Oromo Ethnic Group in Southwestern Ethiopia. *J. Ethnobiol. Ethnomed.* 2008, 4, 11. [CrossRef]

63. Hassan-Abdallah, A.; Merito, A.; Hassan, S.; Aboubaker, D.; Djama, M.; Asfaw, Z.; Kelbessa, E. Medicinal Plants and Their Uses by the People in the Region of Randa, Djibouti. *J. Ethnopharmacol.* 2013, 148, 701–713. [CrossRef] [PubMed]

64. Abdela, G.; Sultan, M. Indigenous Knowledge, Major Threats and Conservation Practices of Medicinal Plants by Local Community in Heban Arsi District, Oromia, South Eastern Ethiopia. *Adv. Life Sci. Technol.* 2018, 68, 19.

65. Cheikhyousef, A.; Shapi, M.; Matengu, K.; Mu Askelehe, H. Ethnobotanical Study of Indigenous Knowledge on Medicinal Plant Use by Traditional Healers in Oshikoto Region, Namibia. *J. Ethnobiol. Ethnomed.* 2011, 7, 10. [CrossRef] [PubMed]

66. Setsbho, M.P.; Mbereki, C.M. Floristic Diversity and Uses of Medicinal Plants Sold by Street Vendors in Gaborone, Botswana. *Afr. J. Plant Sci. Pharm.* 2013, 6, 9–74.

67. Vergiat, A.M. Plantes magiques et médicinales des Féticheurs de l’Oubangui (Région de Bangui). *J. Agric. Tradit. Bot. Appliquée 1969*, 16, 335–367.

68. Al-Fatimi, M. Ethnobotanical Survey of Medicinal Plants in Central Abyan Governorate, Yemen. *J. Ethnopharmacol.* 2019, 241, 11973. [CrossRef]

69. Mothana, R.A.A.; Abdo, S.A.A.; Hasson, S.; Althawah, F.M.N.; Alaghbari, S.A.Z.; Lindequist, U. Antimicrobial, Antioxidant and Cytotoxic Activities and Phytochemical Screening of Some Yemeni Medicinal Plants. *Evid. Based Complement. Altern. Med.* 2010, 7, 323–330. [CrossRef]

70. Desta, B. Ethiopian Traditional Herbal Drugs. Part III: Anti-Fertility Activity of 70 Medicinal Plants. *J. Ethnopharmacol.* 1994, 44, 199–209. [CrossRef]

71. Suryawanshi, V. Extraction and Isolation of Clerodane as a Bioactive Molecule from Tragia Ramosa. *J. Pharmacogn. Phytochem.* 2019, 8, 1135–1138.

72. Welcome, A.K.; Wyk, B.-E.V. An Inventory and Analysis of the Foods of Southern Africa. *S. Afr. J. Bot.* 2019, 122, 136–179. [CrossRef]

73. Magwede, K.; van Wyk, B.-E.; van Wyk, A.E. An Inventory of Vhavenda Useful Plants. *S. Afr. J. Bot.* 2019, 122, 57–89. [CrossRef]
Plants 2021, 10, 2717

74. Agbor, G.A.; Ndjib, R. Systematic Review of Plants Used Against Respiratory Diseases Related to COVID-19 in Africa. *J. Drug Deliv.* **2021**, *11*, 141–153. [CrossRef]

75. Amusan, O.O. Some Ethnomedicines Used for HIV/AIDS and Related Diseases in Swaziland. *Afr. J. Plant Sci. Biotechnol.* **2009**, *3*, 20–26.

76. Ogundare, A.O.; Olorunfemi, O.B. Antimicrobial Efficacy of the Leaves of Dioclea Reflexa, Mucuna Pruriens, Ficus Asperifolia and *Tragia spathulata*. *Res. J. Microbiol.* **2007**, *2*, 392–396. [CrossRef]

77. Tabuti, J.R.S.; Kukunda, C.B.; Waako, P.J. Medicinal Plants Used by Traditional Medicine Practitioners in the Treatment of Tuberculosis and Related Illments in Uganda. *J. Ethnopharmacol.* **2010**, *127*, 130–136. [CrossRef] [PubMed]

78. Silberbauer-Gottsberger, I. O Cerrado Como Potencial de Plantas Medicinais e Tóxicas. *Oréides* **1982**, *8*, 15–30.

79. Ouöba, P.; Lykke, A.; Boussim, J.; Guinko, S. La flore médicale de la Forêt Classée de Niangoloko (Burkina Faso). *Etudes Flor Vég Burkina Faso* **2006**, *10*, 5–16.

80. Reko, B. La Hierba de Quetzalcoatl. *Bot. Sci.* **1946**, *4*, 13–14. [CrossRef]

81. Jiofack, T.; Fokunang, C.; Guedje, N.; Kemeuze, V.; Fongnzossie, E.; Nkongmeneck, B.A.; Mapongmetsem, P.M.; Tsabang, N. Ethnobotanical Uses of Medicinal Plants of Two Ethnoecological Regions of Cameroon. *Int. J. Med. Med. Sci.* **2010**, *2*, 60–79.

82. Arnason, T.; Uck, F.; Lambert, J.; Hebda, R. Maya Medicinal Plants of San Jose Succotz, Belize. *J. Ethnopharmacol.* **1980**, *2*, 345–364. [CrossRef]

83. Seukep, J.A.; Ngadjui, B.; Kuete, V. Antibacterial Activities of Fagara Macrophylla, Canarium Schweinfurthii, Myrianthus Arboreus, Dishistocalyx Grandifolius and *Tragia benthamii* against Multi-Drug Resistant Gram-Negative Bacteria. *SpringerPlus* **2015**, *4*, 567. [CrossRef] [PubMed]

84. Anthoney, S.T.; Ngule, M.C.; Jackie, O.K. In Vitro Antibacterial Activity of Methanolic-Aqua Extract of *Tragia Brevipes* Leaves. *Int. J. Pharm. Sci.* **2014**, *5*, 3289–3294.

85. Chepng’etich, J.; Ngule, C.; Jepkorir, M.; Mwangangi, R.; Njuguna, D.; Ndung’u, J.; Kiboi, D.; Mwitari, P. Total Phenolic Content and in Vitro Antiproliferative Activity of *Tragia Brevipes* (Fam) and Tetradenia Riparia (Hochst) Leaves Extract. *Eur. J. Med. Plants* **2018**, *22*, 1–10. [CrossRef]

86. Sivajothi, V.; Dakappa, S.S. In Vitro and in Silico Antidiabetic Activity of Pyran Ester Derivative Isolated from *Tragia Cannabina*. *Asian Pac. J. Trop. Biomed.* **2014**, *4*, S455–S459. [CrossRef] [PubMed]

87. Gupta, S.M.; Kumar, K.; Dwivedi, S.K.; Bala, M. Bioactive Potential of Indian Stinging Plants Leaf Extract against Pathogenic Fungi. *J. Complement. Integr. Med.* **2019**, *16*, 20170125. [CrossRef]

88. Perumal Samy, R.; Manikandan, J.; Al Qahtani, M. Evaluation of Aromatic Plants and Compounds Used to Fight Multidrug Resistant Infections. *Evid. Based Complement. Altern. Med.* **2013**, *2013*, 1–17. [CrossRef]

89. Thomas, R.; Megha, K.; Surya, P.; Rosaline, T.; Varghese, S.; Elyas, K. Investigation on the Biological Attributes of *Tragia involucrata* Linn. Using in Vitro Methods. *J. Pharmacogn. Phytochem.* **2021**, *10*, 398–404. [CrossRef]

90. Velu, V.; Das, M.; Raj, N.A.N.; Dua, K.; Malipeddi, H. Evaluation of in Vitro and in Vivo Anti-Urolithiatic Activity of Silver Nanoparticles Containing Aqueous Leaf Extract of *Tragia involucrata*. *Drug Deliv. Transl. Res.* **2017**, *7*, 439–449. [CrossRef] [PubMed]

91. Niyva, M.T.; Patil, R.K.; Rao, G.M.A.; Khandagale, A.; Somashekarappa, H.; Ananda, D.; Manjunath, H.; Joshi, C.G. Cytotoxicity and Antitumor Activity of Hexane and Ethyl Acetate Extracts of *Tragia involucrata*. *Int. J. Cancer Res.* **2011**, *7*, 60–79. [CrossRef] [PubMed]

92. Leonti, M.; Casu, L. Ethnopharmacology of Love. *J. Complement. Integr. Med.* **2011**, *22*, 567. [CrossRef] [PubMed]

93. Attah, A.F.; Omobola, A.I.; Moody, J.O.; Sonibare, M.A.; Adebukola, O.M.; Onasawo, S.A. Detection of Cysteine-Rich Peptides in *Tragia benthamii* Baker (Euphorbiaceae) and in Vivo Antiinflammatory Effect in a Chick Model. *Phys. Sci. Rev.* **2021**, *10151520200125*, 1–10. [CrossRef]

94. Bhattacharya, K.; Chandra, G. Phagodeterrence, Larvicidal and Oviposition Deterrence Activity of *Tragia involucrata* L. (Euphorbiaceae) Root Extractives against Vector of Lymphatic Filariasis Culex Quinquefasciatus (Diptera: Culicidae). *Asian Pac. J. Trop. Dis.* **2014**, *4*, S226–S232. [CrossRef]

95. Subramani, P.; Sampathkumar, N.; Ravindiran, G.; Rajalingam, D.; Kumar, B. Evaluation of Nephroprotective and Antioxidant Potential of *Tragia involucrata*. *Drug Invent. Today* **2009**, *1*, 55–60.

96. Joshi, C.G.; Gopal, M.; Kumari, N. Antitumor Activity of Hexane and Ethyl Acetate Extracts of *Tragia involucrata*. *Int. J. Cancer Res.* **2011**, *7*, 267–277. [CrossRef]

97. Islam, M.S.; Sana, S.; Haque, M.E.; Rahman, S.M.M.; Samad, A.; Noman, A.A.; Alam, R.; Rana, S.; Meem, R.I.; Mondol, D.; et al. Methanol, Ethyl Acetate and n-Hexane Extracts of *Tragia involucrata* L. Leaves Exhibit Anxiolytic, Sedative and Analgesic Activity in Swiss Albino Mice. *Heliyon* **2021**, *7*, e05814. [CrossRef]

98. Samy, R.P.; Gopalakrishnakone, P.; Houghton, P.; Ignacimuthu, S. Purification of Antibacterial Agents from *Tragia involucrata*—A Popular Tribal Medicine for Wound Healing. *J. Ethnopharmacol.* **2006**, *107*, 99–106. [CrossRef]

99. Varma, G.G.; Mathai, B.K.; Das, K.; Gowda, G.; Rammohan, S.; Einstein, J.W. Evaluation of Antiepileptic Activity of Methanolic Leaves Extract of *Tragia involucrata* Linn. in Mice. *Int. Lett. Nat. Sci.* **2014**, *12*, 167–179. [CrossRef]

100. Thimmaiah, N.; Joshi, C.; Patil, R.; Khandagale, A.; Somashekarappa, H.; Ananda, D.; Manjunath, H. Mitigation of Radiation-Induced Oxidative Stress by Methanolic Extract of *Tragia involucrata* in Swiss Albino Mice. *Pharmacogn. Res.* **2019**, *11*, 236. [CrossRef]
101. Dhara, A.K.; Suba, V.; Sen, T.; Pal, S.; Chaudhuri, A.K.N. Preliminary Studies on the Anti-Inflammatory and Analgesic Activity of the Methanolic Fraction of the Root Extract of *Tragia involucrata* Linn. *J. Ethnopharmacol.* **2000**, *72*, 265–268. [CrossRef] [PubMed]

102. Samy, R.P.; Gopalakrishnakone, P.; Sarumathi, M.; Ignacimuthu, S. Wound Healing Potential of *Tragia involucrata* Extract in Rats. *Fitoterapia* **2006**, *77*, 300–302. [CrossRef] [PubMed]

103. Dhara, A.K.; Pal, S.; Nag Chaudhuri, A.K. Psychopharmacological Studies on *Tragia involucrata* Root Extract. *Phytother. Res.* **2002**, *16*, 326–330. [CrossRef]

104. Samy, R.P.; Gopalakrishnakone, P.; Houghton, P.; Thwin, M.M.; Ignacimuthu, S. Effect of Aqueous Extract of *Tragia involucrata* Linn. on Acute and Subacute Inflammation. *Phytother. Res.* **2006**, *20*, 310–312. [CrossRef]

105. Sama, V.; Rajini, T.; Afrooz, H.; Balaraju, P.; Reddy, B.M.; Mullangi, R. Antihyperglycemic Effects of *Tragia Plukenetii* Ethanol Extract. *Int. J. Pharm. Sci. Nanotechnol.* **2014**, *7*, 2436–2440. [CrossRef]

106. Kalaivanan, M.; Jesudass, L. Pharmacological Studies on Ethanol Extract of *Tragia Plukenetii* R. Smith. *IOSR J. Pharm.* **2012**, *2*, 1–7.

107. Muthuraman, M.; Dorairaj, S.; Rangarajan, P.; Pemaiah, B. Antitumor and Antioxidant Potential of *Tragia Plukenetii* R. Smith on Ehrlich Ascites Carcinoma in Mice. *Afr. J. Biotechnol.* **2008**, *7*, 3527–3530.

108. Manoharan, S.K. Evaluation of Anticonvulsant Activity of *Tragia Plukenetii* R. Smith Leaf Extracts against Chemoshock Induced by Pentylentetrazole in Mice. *Res. J. Pharm. Biol. Chem. Sci.* **2015**, *6*, 750–753.

109. Altemimi, A.; Lakhssassi, N.; Baharlouei, A.; Watson, D.; Lightfoot, D. Phytochemicals: Extraction, Isolation, and Identification of Bioactive Compounds from Plant Extracts. *Plants* **2017**, *6*, 42. [CrossRef]

110. Thangiah, A.S.; Mutuku, N.; Ngule, E.; Francis, R. Qualitative Analysis of Phytoconstituents in *Tragia Brevipes* Plant. *Int. J. Pharm. Res. Anal.* **2018**, *3*, 93–98.

111. Antony, C. Phytochemical and Spectral Study of the Medicinal Plant: *Tragia Plukenetii*. *J. Pharm. Res.* **2012**, *5*, 1701–1703.

112. Olaoye, S.B.; Ibrahim, A.O.; Zhiqiang, L. Chemical Compositions and Radical Scavenging Potentials of Essential Oils from *Tragia benthamii* (BAKER) and *Cissus Aralioides* (WELW). *J. Biol. Act. Prod. Nat.* **2016**, *6*, 59–64. [CrossRef]

113. Gobalakrishnan, R.; Kulandaivelu, M.; Bhuvaneswari, R.; Kandavel, D.; Kannan, L. Screening of Wild Plant Species for Antibacterial Activity and Phytochemical Analysis of *Tragia involucrata* L. *J. Pharm. Anal.* **2013**, *3*, 460–465. [CrossRef] [PubMed]

114. Balogun, O.S.; Oladosu, I.A.; Liu, Z. Isolation of 2, 5-Dithia-3, 6-Diazabicyclo [2.2.1] Heptane and GC-MS Analysis of Silylated Extract from *Tragia benthamii*. *Ife J. Sci.* **2020**, 22, 75–80. [CrossRef]

115. Alagar Yadav, S.; Ramalingam, S.; Jabamalai Raj, A.; Subban, R. Antihistamine from *Tragia involucrata* L. Leaves. *J. Complement. Integr. Med.* **2015**, *12*, 217–226. [CrossRef] [PubMed]