The genus *Eriosema* (Fabaceae): From the Ethnopharmacology to an Evidence-Based Phytotherapeutic Perspective?

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The genus *Eriosema* (Fabaceae) includes approximately 150 species widely distributed across tropical and subtropical regions of the world (Africa, Neotropics, Asia and Australia). Throughout these regions, several species are used since centuries in different traditional medicinal systems, while others are used as food or food supplement. The present review attempts to critically summarize current information concerning the uses, phytochemistry and pharmacology of the *Eriosema* genus and to evaluate the therapeutic potential. The information published in English and French (up to September 2020) on ethnopharmacology or traditional uses, chemistry, pharmacology and toxicology of *Eriosema* genus was collected from electronic databases [SciFinder, PubMed, Google, Google Scholar, Scopus, Web of Science, Prelude Medicinal Plants—http://www.ethnopharmacologia.org/recherche-dans-prelude/?plant, The Plant List (http://www.thepointlist.org/), POWO (http://powo.science.kew.org/) and IUCN Red List Categories (https://www.iucnredlist.org/)], conference proceedings, books, M.Sc. and Ph.D. dissertations. The information retrieved on the ethnomedicinal indications of *Eriosema* genus allowed to list 25 species (∼16.6% of the genus). The majority of uses is recorded from Africa. Phytochemical analyses of 8 species led to the identification and/or isolation of 107 compounds, with flavonoids (69.2%), chromones (7.5%) and benzoic acid derivatives (3.7%) as the main chemical classes. Pharmacological investigations with crude extracts and isolated compounds showed a broad range of activities including aphrodisiac, estrogenic, anti-osteoporosis, hypolipidemic, anti-diabetic, anti-diarrheal, anti-microbial, anti-oxidant, anthelmintic, anti-cancer, and acetylcholinesterase inhibitory activities. Despite the low number of *Eriosema* species tested, there is convincing evidence in vitro and in vivo studies validating some traditional and ethnobotanical uses. However, the utility of several of the described uses has not yet been confirmed in pharmacological studies. Reviewed data could serve as a reference tool and preliminary information for advanced research on *Eriosema* species.

Keywords: *Eriosema*, Fabaceae, pharmacological activities, phytochemistry, ethnopharmacology, toxicology
INTRODUCTION

Eriosema (Fabaceae), with approximately 150 species of shrubs, shrublets and herbs, is the second-largest genus of the Cajaneae subtribe (Ma et al., 1995; LPWG, 2017). This monophyletic clade originated in the late Miocene and its diversification occurred in parallel with the savanna biome expansion around the world (Cândido et al., 2020). The current centers of diversity and endemism of Eriosema species include the grasslands, wooded savanna and waste places of Africa (West, Central, East and South Africa), Central America (from Mexico to northern Argentina, except for Chile), Southeast Asia and Northern Australia (Wu, 1991; Schrire et al., 2005; Cândido et al., 2019). The African species are most abundant (nearly 110 species) and the first diverging evolution suggests an African origin of the genus (Cândido et al., 2020). The study by Cândido et al. (2019) recorded 35 Eriosema species in Brazil, which encompasses 85% of the diversity of the genus in the Americas (35 out of 41 species).

Throughout this pantropical region, several Eriosema species are intensively used in traditional medicine and for non-medicinal purposes (e.g. food/vegetables, toothbrush). Based on the traditional uses, phytochemical, pharmacological and toxicological investigations of different Eriosema species have been performed. Nevertheless, till now only few reviews dealing with Eriosema species have been published. The studies by Cândido et al. (2019, 2020), respectively, focused on the taxonomic synopsis of Eriosema in Brazil and molecular phylogenetic insights into the evolution of Eriosema. In 2015, Awouafack et al. demonstrated that Eriosema species represent a rich source of flavonoids with interesting pharmacological activities. In this review, authors compiled a total of 52 flavonoids (isoflavones, dihydroflavonols, isoflavonones, flavanols, flavones, and dihydrochalcones) isolated from Eriosema species. However, the pharmacological properties are not limited to the flavonoids. In the literature, compounds from other chemical classes as well as plant extracts (more easily available and affordable than isolated compounds) demonstrated pharmacological properties. More recently, the review of Kleyhans et al. (2020) focused on Eriosema kraussianum Meissn. None of these reviews presented the global overview on the traditional uses, phytochemistry, pharmacological properties and toxicological evaluation of this genus. Accordingly, the present review attempts to critically summarize the available information on the traditional uses, phytochemistry, and pharmacological activities as well as safety evaluation of the genus Eriosema and, therefore, to evaluate the data for potential phytotherapeutic approaches.

SEARCH STRATEGY AND TERMS USED

The information on the genus Eriosema published up to September 2020 in English and French was collected from different electronic data bases (SciFinder including Chemical Abstracts and Medline, PubMed, Google, Google Scholar, Scopus, Web of Science), conference proceedings, books, M.Sc. and Ph.D. dissertations. The keywords “Eriosema” in conjunction with ‘traditional uses’ or ‘ethnopharmacology,’ ‘phytochemistry,’ ‘pharmacology,’ and ‘toxicology’ were used. In addition, Prelude Medicinal Plants (http://www.ethnopharmacologia.org/recherche-dans-prelude?plant), The Plant List (http://www.theplantlist.org/) and POWO (http://powo.science.kew.org/) were explored for the plant’s traditional uses and scientific names, while information on the global extinction risk status of Eriosema species was gathered from the IUCN (International Union for Conservation of Nature) Red List Categories (https://www.iucnredlist.org/).

TRADITIONAL USES AND ETHNOPHARMACOLOGY OF ERIOSEMA SPECIES

Since centuries, Eriosema species have widely been traditionally used as household remedies against various human ailments. Accordingly, in the pharmaceutical landscape this genus may represent a remarkable source of promising substances. From the literature review, various medicinal and contemporary uses associated with this genus are summarized in Table 1.

According to South African Zulu traditional health practitioners, the roots of several Eriosema species such as Eriosema kraussianum N. E. Br., Eriosema salignum E. Mey. and Eriosema cordatum E. Mey., known under the indigenous umbrella name of uBangledala, are effective to cure or alleviate erectile dysfunction (ED) and/or impotence (Bryant, 1966; Hutchings et al., 1996; Ojewole et al., 2007; Drewes et al., 2013). In Southern and Eastern Africa, they are also used as expectorants and diuretics (Watt and Breyer-Brandwijk, 1962). In case of impotence, hot milk infusions of the plants’ roots and/or pounded boiled root decoctions are taken at small doses twice a day (Hulme, 1954; Bryant, 1966). Studies reported that the roots of E. cordatum are used for male (Hutchings et al., 1996) and female (Bryant, 1966) infertilities and as constituent of Imbiza ephuzwato, a Zulu traditional herbal medicine (Van Wyk et al., 1997). This mixture is used as tonic, against anxiety, for clearing skin conditions, to treat diabetes mellitus, kidney and urinary infections, tonsillitis, pneumonia, constipation, stomach and back pains, for the improvement of high blood pressure, to boost energy, vitality and sexual activity as well as in the prevention of arthritis (Ndhlala et al., 2011).

In Angola, fresh leaves of Eriosema glomeratum (Guill. & Perr.) Hook. f. are eaten as food/vegetables and administered against diarrhea and dysentery (Göhre et al., 2016; Lautenschläger et al., 2018). In Benin, they are used against diabetes (Lawin et al., 2015), while the leafy stem is claimed to promote the closure of fistulation (Adomou et al., 2012). The roots are applied in Burkina Faso against hernia (Ouoba et al., 2006). In the Bakola Pygmy tribe, the whole plant is used for many purposes including pulmonary troubles, nasopharyngeal infections, leprosy and venerable diseases (Verdcourt, 1970).

Indians around Kunana (Venezuela) use the root decoction of Eriosema rufum G. Don. against sterility in women and to accelerate delivery in childbirth (Morton, 1981).
| Species | Parts used | Location | Local and traditional uses | Preparation | References |
|---------|------------|----------|----------------------------|-------------|------------|
| Eriosema affine De Wild. | Roots | Angola (Bié province) | Malaria, stomach pain, diarrhea | Decoction | Novotna et al. (2020) |
| | | Angola | Prevention of abortion, chest pain, malaria, vomiting, nightmares, epilepsy, flu | Not specified | Bossard (1996) |
| Eriosema benthamianum Mart. ex Benth. | Roots | Brazil | Inflammation | Not specified | Hirschhorn (1982) |
| Eriosema burkei Benth. ex Harv. & Sond. | Roots | Brazil (Brazilian Cerrado) | Inflammatory diseases e.g. inflammatory skin disorders such as psoriasis | Decoction | Santos et al. (2016) |
| Eriosema chinense Vogel (syn. Eriosema himalaicum H. Ohashi or Eriosema tuberosum (Ham.) Wang et Tang) | Roots | Northern Australia, China, North East of India | Food/vegetable, diarrhea | Consumption of fresh roots | Neogi et al. (1989); Martin and Ryan (2004); Prasad et al. (2013c) |
| | Seeds, leaves | India (Meghalaya) | Diarrhea, wounds, astringent, diuretic, tonic, cold sweats, and parturition (promoting discharge of lochia) | Decoction | Prasad et al. (2013c), Ashraf and Borthakur (2005), Laio and Hemalatha (2011), Thongnest et al. (2013) |
| | Seeds | Thailand (central region of Myanmar) | Scrofula, diabetes, leucorrhoea, menstrual problems | Decoction | Aye et al. (2019) |
| | Leaves | Republic of Congo | Wound healing and diuretic | Decoction | Thongnest et al. (2013) |
| | | | Male infertility, erectile dysfunction, impotence | Hot milk infusion; decoction | Drewes et al. (2002), Drewes et al. (2004), Bryant (1966), Hutchings et al. (1996) |
| Eriosema cordatum E.Mey | Roots | South Africa | Unspecified female diseases | Not specified | Hastings (1990) |
| | | | Abortive, contraceptive | Eye instillation of fresh leaves’ juice | Rodrigues (2007) |
| | Leaves | Mexico (Guatemala) | Bilharziosis | Not specified | Mmbengwa et al. (2009) |
| | | | Dietary supplement | Consumption of fruits | Mbogo (1990) |
| Eriosema englerianum Harms | Roots | Zimbabwe | Diabetes | Not specified | Akendengué and Louis (1991) |
| | Leaves | South Africa (Ngoni province) | Diarrhea, dysentery, cholera, shigellosis | Consumption of fresh leaves | Lautenschläger et al. (2018) |
| | | Benin (Sudano-Guinean zone) | Food/vegetables | Consumption of fresh leaves, tea | Göhre et al. (2016) |
| | Leaves | Angola (Bakongo tribes) | Vertigo fainting, syncope, delayed closure of fontanel | Maceration | Adomou et al. (2012) |
| | | Angola (province of Uige) | Hernia | Maceration (bath) | Ouedraogo et al. (2006) |
| | | Benin | Pulmonary troubles, mucosal infections, nasopharyngeal infections, leprosy, skin infections, venereal diseases | Maceration, dried, pounded roots in coffee or porridge | Verdcout (1970) |
| Eriosema griseum Baker | Leaves | Ivory Coast | Parasitic diseases associated with stomach ache, dysentery, diarrhea in children | Not specified | Koné et al. (2005), Koné et al. (2012) |
| Eriosema hirsuta (Bent.) Hook.f | Roots | South Africa | Erectile dysfunction, impotence, urinary complaints in males | Hot milk infusion of roots; maceration of root bark | Drewes et al. (2002), Drewes et al. (2004), Bryant (1966), Hutchings et al. (1996) |

(Continued on following page)
| Species | Parts used | Location | Local and traditional uses | Preparation | References |
|---------|------------|----------|----------------------------|-------------|------------|
| *Eriosema laurentii* De Wild. | Leaves | West Africa | Food/vegetable, nervous disorders, laxative, leprosy, nasopharyngeal affections, pulmonary problems, skin diseases, mucosal infections, venereal diseases, fish-poison | Not specified | Burkill (1985) |
| | Leaves, roots | Cameroon | Infertility, gynecological and menopausal complaints | Decoction | Ateba et al. (2013b) |
| *Eriosema lebrunii* Staner & De Craene | Leaves | Burundi | Skin diseases, eczema, impetigo, dermatoses, ringworm, fungal infections, athlete’s foot, urticaria | Application of juice of fresh leaves on the infection site | Ngezahayo et al. (2015) |
| *Eriosema montanum* Bak. f. | Not specified | Democratic Republic of Congo | Wound healing, antimicrobial, disinfectant | Not specified | Kasonia et al. (1991) |
| | Leaves | Burundi | Injuries | Application of pounded fresh or dry leaves on the injury | Byavu et al. (2000) |
| | | | Oxytocic during childbirth | Decoction | Lewalle and Rodegem (1968) |
| | | | Impotence, anemia, vitamin deficiency, delayed motor development, vitality, metronorphagia, overwork, tonic | Decoction, maceration, enema | Polygenis-Bigendako (1990); Baerts and Lehmann (1989) |
| | | | Otitis, mumps, deafness, earache, otorhea | Ear instillation of fresh leaves’ juice | polygenis-Bigendako (1990); Van Puyvelde et al. (1977) |
| | | | Snake bite, sting of poisonous animals | Application of pounded leaves at the bite site, decoction | polygenis-Bigendako (1990); Fumba (1983); Van Puyvelde et al. (1977); Baerts and Lehmann (1989) |
| | | | Skin diseases (ringworm, mycosis, dermatosis, eczema) | Consumption of calcined dried leaves | Ngezahayo et al. (2015) |
| | | | Diarrhea, dysentery, cholera | Decoction, enema | Ngezahayo et al. (2015); Baerts and Lehmann (1989) |
| | | | Joint pain, inflammation, rheumatism | Macerate; vigorous local rubbing of leaves | Van Puyvelde et al. (1977) |
| | | | Eye diseases | Eye instillation of fresh leaves’ juice | Baerts and Lehmann (1989) |
| | | | Sprain, hematoma, strain, dislocation, contusion, fracture | Local application of pounded fresh leaves | Baerts and Lehmann (1989) |
| | | | Palpitation, heart pain | Not specified | |
| | | | Pulmonary problems, cough, fever, vomiting, nausea, anxiety, epilepsy, depression, nervous disorders, mental illnesses, anagistic | Decoction, steam bath | |
| | | | Rwanda | Snake-bites, cough, conjunctivitis | Not specified | Baerts and Lehmann (1989); Rwangabo (1993) |
| | Roots | Rwanda | Pulmonary problems, cough | Consumption of raw roots | Durand (1960) |
| *Eriosema parviflorum* E.Mey. | Leaves, bark, roots | Tanzania (Kagera and Lindi regions) | Malaria | Decoction, juice of fresh leaves | Nondo et al. (2015); Moshi et al. (2010) |
| *Eriosema psoraleoides* (Lam.) G.Don | Twigs | Tanzania (Morogoro) | Tooth brush | Not specified | Khan et al. (2000) |
| | Stem bark | Democratic Republic of Congo (Kinshasa) | Tuberculosis | Decoction | Ngbolou et al. (2014) |
| | | Central African Republic | Laxative | Not specified | Sandberg (1965) |
| | | Central African Republic | | | |
| | | Congo | | | |
| | | Leaves | Tanzania (Bukoba rural district) | Health problems related to HIV/AIDS such as chronic diarrhea | Not specified | Kisangau et al. (2007) |
| | | Central Africa | Oxytocic during childbirth | Water extract | Sillans (1953) |
| | | West Africa | Ectoparasites | Rubbing locally | Daziel (1937) |

(Continued on following page)
### TABLE 1 | (Continued) Ethnomedicinal indications and local uses of *Eriosema* species based on the literature data review.

| Species                  | Parts used | Location                          | Local and traditional uses                          | Preparation                   | References                        |
|--------------------------|------------|-----------------------------------|-----------------------------------------------------|------------------------------|-----------------------------------|
| Central African Republic | Endoparasites (cestodes, nematodes, tapeworms, amoebiasis) | Decoction | Wome (1985), Sillans (1953) |
|                          | Diarrhea, dysentery | Maceration | Haixaire (1979) |
|                          | Vaginal prolapse, wound healing | Fumigation | Haixaire (1979), Descoings (1963) |
|                          | Eye diseases | Not specified | Descoings (1963) |
|                          | Eye diseases | Maceration (eyewash) | Maizy (1954) |
|                          | Expectorant | Decoction | Goossens (1924) |
| Cameroon Democratic Republic of Congo | Fish-poison | Not specified | Goossens (1924) |
|                          | Eye diseases | Eye instillation of fresh leaves’ juice | Wome (1985) |
|                          | Wound healing | Application of pounded dried leaves on the wound | Nyakabwa and Gapusi (1990) |
|                          | Abscess, boil, ulcer, acne | Local application of pounded fresh leaves | Nyakabwa and Gapusi (1990) |
|                          | Sexually transmitted diseases, expectorant | Decoction | Staner and Boutique (1937) |
| Ivory Coast, Burkina Faso Benin | Skin diseases | Eye instillation of fresh leaves’ juice | Kerharo and Bouquet (1950) |
|                          | Nigeria Rwanda Burundi | Skin diseases, fever, malaria | Local application of fresh leaves’ juice | Verger (1995) |
|                          | | Skin diseases | Decoction | Adjanohoun et al. (1991) |
|                          | | Abdominal pain, gastritis, stomach aches | Decoction | Desouter (1991) |
|                          | | Tonic | Leaf juice | Baerts and Lehmann (1989) |
|                          | | Water extract | Haerdi (1964) |
| Democratic Republic of Congo | Miscarriage in combination with *Pilostigma trioningia* | Ear instillation of fresh leaves’ juice | Boulesteix et al. (1979) |
| Uganda | | | | |
| Rwanda Burundi Kenya Tanzania Roots, leaves | Stomach ache, gastritis, colic, colitis, stomach ulcer | Consumption of roots | Durand (1960) |
| | | | | Baerts and Lehmann (1989) |
| | | | | Masinde (1996) |
| | | Abdominal pain, gastritis, stomach aches | Decoction | |
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Eriosema robustum Baker is widespread in Burundi, Ethiopia, Kenya, Rwanda, Tanzania, Uganda, Democratic Republic of Congo and Cameroon (Gillett et al., 1971). It is believed to cure coughs in East Africa (Kokwaro, 2009) and skin diseases in Central Africa (Awouafack et al., 2013a).

Eriosema laurentii De Wild. widely dispersed in West and Central Africa is used in this area as food and herbal medicine for many purposes such as nasopharyngeal, brain and nervous system affections, pulmonary troubles and venereal diseases (Burkill, 1985). In Cameroon, the plant is utilized for the treatment of infertility and various gynecological problems (Ateba et al., 2013).

The roots of Eriosema chinense Vogel (syn. Eriosema himalaicum H. Ohashi; Eriosema tuberosum (Ham.) Wang et Tang) are reported to be used as food in Northern Australia, China and North East India and against diarrhea in Meghalaya (India) (Neogi et al., 1989; Martin and Ryan, 2004; Prasad et al., 2013a). In Yunnan Province of China, the roots are used against diarrhea, orchitis, hydrophobia and as detoxifying medicine (Kunming Institute of Botany, 1979). In Thailand, the fresh roots are eaten as a tonic, and decoctions of the seeds are used for wound healing and for their diuretic properties (Thongnest et al., 2013). Such decoctions are also well-known as an astringent, diuretic, tonic, against cold sweats and during delivery to promote discharge of the lochia. Decoctions additionally containing powdered pepper are given for diarrhea (Ashraf and Borthakur, 2005; Laloo and Hemalatha, 2011; Prasad et al., 2013c; Thongnest et al., 2013).

Eriosema psoraleoides (Lam.) G. Don. is a species widely used over Africa from Togo to Tanzania. In Tanzania, peeled or unpeeled twigs are used as chewing sticks (Khan et al., 2000), while leaves are used against health problems related to HIV/AIDS such as chronic diarrhea (Kisangau et al., 2007), impotence, erectile dysfunction, fever and malaria (Moshi et al., 2009, 2010). In several countries in Central and West Africa, leaves are applied against eye diseases (Kerharo and Bouquet, 1950; Malzy, 1954; Descoings, 1963; Wome, 1985). The roots are used in Central African Republic against ear pains (Boulesteix and Guinko, 1979), and in Democratic Republic of Congo and Burundi against sexually transmitted diseases (Staner and Boutique, 1937; Baerts and Lehmann, 1989). Eating raw roots is claimed to treat pulmonary problems in Rwanda (Durand, 1960).

Leaves of Eriosema griseum Baker are known as infant cures for treating parasitic diseases and associated discomforts such as stomach ache, dysentery or diarrhea in Northern parts of Ivory Coast (Koné 2005; Koné et al., 2012).

The roots of Eriosema engleriannum Harms are traditionally used in Zimbabwe in combination with other plants such as Vigna unguiculata and Terminalia sericea to treat bilharziosis (Mmbengwa et al., 2009).

In southeastern Brazil (Cerrado of Minas Gerais), Eriosema glabrum Mart. ex Benth. is a traditional laxative, while Eriosema benthamianum Mart. ex Benth. and Eriosema campestre var. macrophyllum (Gear) Fortunato are reported as anti-inflammatory agents (Hirschmann and De Arias, 1990).

Globally, the search of information resulted in 25 species (~16.6% of the genus), for which written evidence of traditional uses is available. Clearly, this list cannot be exhaustive as in many traditional medicine systems a vast knowledge on medicinal plants exists as oral information only. The majority of medicinal plants used over the world are harvested from wild resources in increasing volumes. Given their integral role in basic healthcare in many developing countries, their conservation and sustainable use are a necessity. The information of the IUCN (International Union for Conservation of Nature) Red List Categories, assessing the conservation status of species, was accessed for Eriosema species from https://www.iucnredlist.org/fr/search?query=Eriosema&searchType=species. At the moment, only 22 Eriosema species (Table 2) are included in this list. Information for the vast majority of species widely used in traditional medicine such as E. chinense, E. cordatum, E. glomeratum and E. psoraleoides and others depicted in Table 1 is still missing. Only the three traditionally used species Eriosema crinitum (Kunth) G. Don, Eriosema engleriannum Harms and Eriosema montanum Baker f. are listed, characterized by a stable population with least concern. Nevertheless, the most popular species with traditional use should be assessed to avoid a negative impact on the size of the populations. Root and whole-plant harvesting is more destructive than collecting leaves and flowers or buds (Chen et al., 2016). Among the 25 species traditionally used and reported in this review, mainly roots are utilized (18 species), followed by leaves (11 species), bark and whole plant (3 species), seeds or fruits (2 species) and twigs (1 species) (Figure 1). Rather to use roots, leaves can be an alternative to avoid the destruction and high-speed disappearing of Eriosema species. In case roots are unavoidable for the use, non-destructive harvest protocols such as partial-root harvest should be applied.

### Table 1 (Continued) Ethnopharmacological indications and local uses of Eriosema species based on the literature data review.

| Species                  | Parts used | Location       | Local and traditional uses                  | Preparation | References |
|--------------------------|------------|----------------|---------------------------------------------|-------------|------------|
| Eriosema salignum E. Mey | Roots, root bark | South Africa | Male sexual disorders, erectile dysfunction, impotence | Hot milk infusion of roots, maceration of root bark | Drewes et al. (2002), Drewes et al. (2013) |
| Eriosema scioanum Avetta | Leaves    | Ethiopia       | Sexually transmitted diseases               | Not specified | Lemordant (1972) |
| Eriosema stanerianum Hauman | Leaves | Uganda (Sango Bay area) | Malaria                                      | Decoction   | Ssegawa and Kasenere (2007) |
| Eriosema tisseranti Staner & De Craene | Roots | Central Africa | Aphrodisiac, erectile dysfunction, Women’s sterility, frigidity | Water extract | Sillans (1953) |

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Eriosema: Ethnopharmacology, Phytochemistry, Pharmacology, Toxicology
TABLE 2 | The International Union for Conservation of Nature (IUCN) Red List Categories of Eriosema species.

| Species                                 | Scope of assessment | Population trend | Date of the last assessment | IUCN red list categories |
|-----------------------------------------|---------------------|------------------|----------------------------|--------------------------|
| Eriosema adamaouense Jacq.-Fel.         | Global              | Decreasing       | March 25, 2011              | CR                       |
| Eriosema adami Jacq.-Fel.               | Global              | Unknown          | December 18, 2018           | CR                       |
| Eriosema arachnoides Verdc.             | Global              | Unknown          | September 03, 2011          | EN                       |
| Eriosema arenicola (Verdc.) Maesen & Weringa | Global              | Unknown          | December 04, 2018          | VU                       |
| Eriosema benguellensis Rossberg         | Global              | Unknown          | June 30, 2010               | DD                       |
| Eriosema betulexanae Du Puy & Labat     | Global              | Decreasing       | September 03, 2015          | EN                       |
| Eriosema crinitum (Kunth) G. Don        | Global              | Stable           | August 13, 2010             | LC                       |
| Eriosema englerianum Harms              | Global              | Stable           | April 23, 2010              | LC                       |
| Eriosema harmsiana Dinter               | Global              | Stable           | April 30, 2004              | LC                       |
| Eriosema latericola Jacq.-Fel.          | Global              | Unknown          | December 19, 2018           | EN                       |
| Eriosema leptozygi Jacq.-Fel.           | Global              | Decreasing       | March 25, 2011              | VU                       |
| Eriosema longicalyx Grear               | Global              | Stable           | September 16, 2010          | LC                       |
| Eriosema montanum Baker f.              | Global              | Stable           | September 03, 2011          | LC                       |
| Eriosema pauciflorum Klotzsch           | Global              | Stable           | July 06, 2016               | LC                       |
| Eriosema procumbens Baker               | Global              | Unknown          | September 01, 2015          | LC                       |
| Eriosema pseudodistinctum Verdc.        | Global              | Unknown          | September 03, 2011          | VU                       |
| Eriosema pseudostolzii Verdc.           | Global              | Unknown          | September 03, 2011          | EN                       |
| Eriosema raynalorum Jacq.-Fel.          | Global              | Unknown          | July 14, 2015               | LC                       |
| Eriosema scipatum Hook.f                | Global              | Unknown          | February 18, 2019           | LC                       |
| Eriosema trifurcatae Schreb.            | Global              | Decreasing       | November 11, 2016           | CR                       |
| Eriosema violaceum (Aubl.) G. Don       | Global              | Stable           | June 12, 2018               | LC                       |
| Eriosema chevaleri (Harms) Hutch. & Dalziel (syn. Rhynchosia chevaleri Harms) | Global              | Unknown          | January 07, 2019            | EN                       |

CR, critically endangered; DD, data deficient; EN, endangered; LC, least concern; VU, vulnerable.

Flavonoids
In their review, Awouafack et al. (2015) compiled a total of 52 natural flavonoids (indicated by (*) in Table 3) from five Eriosema species (E. chinense, E. tuberosum, E. kraussianum, E. glomeratum and E. robustum), including dihydrochalcones (1–2), flavonols (10–13, 16–20), flavanons or dihydroflavanons (23–33), flavanones (34–41), isoflavones (43, 47–52, 54, 56–60, 62, 64–70) and one isoflavanone (71). Flavonoids/iso flavonoids not recorded in that review and/or from different Eriosema species are mentioned below.

In a dereplication approach, the flavones isovitexin (3), luteolin (6), isoorientin (7) and luteolin-7-O-glucoside (8) were unambiguously identified in a methanol extract of the aerial parts of E. laurentii (Ateba et al., 2014b) and 2′-O-α-l-rhamnosyl-6-C-fucosyl-3′-O-methyl-luteolin (9) was isolated from the same extract (Ateba et al., 2016a). Vitexin (4) and robus flavone C (5) were extracted from an ethanol fraction of twigs of E. robustum (Awouafack et al., 2018).

The flavonol kaempferol (10) was isolated from roots of E. chinense (Thongnest et al., 2013) and twigs of E. robustum (Awouafack et al., 2018).

Quercetin (13) and quercetin-3-O-methylether (14) were identified in a methanol extract of the aerial parts of E. laurentii (Ateba et al., 2014b), while 3′,4′,6,8-tetrahydroxyflavon-7-C-glucoside (15) from that extract was identified for the first time in the genus (Ateba et al., 2016a).

The flavanons 3′,4′,6,8-tetrahydroxyflavanone-7-C-glucoside (21) and (25,35)-6,8,3′-triprenyl-dihydromorin (22) from the methanol extracts of the aerial (Ateba et al., 2016a) and underground (Ateba et al., 2016b) parts of E. laurentii,
| Chemical classes              | N° | Compounds                                                                 | Plant parts and species               | References                                      |
|------------------------------|----|---------------------------------------------------------------------------|---------------------------------------|------------------------------------------------|
| **Dihydrochalcones**         |    | Eriochalcone a or 2',4'-dihydroxy-4'-methoxy-3'-(y,y-dimethylallyl) dihydrochalcone (*) | Whole plant of *E. glomeratum*         | Awouafack et al. (2008)                         |
|                              |    | Eriochalcone B or 2',4'-dihydroxy-3'-y,y-dimethylallyl dihydrochalcone (*) | Whole plant of *E. glomeratum*         | Awouafack et al. (2008)                         |
| Flavones                     |    | Isovitexin or Apigenin-6-C-glucoside                                      | Aerial parts of *E. laurentii*         | Awouafack et al. (2014b)                        |
|                              |    | Vitexin                                                                   | Twigs of *E. robustum*                | Thongnest et al. (2013)                         |
|                              |    | Robustiflavone C                                                          | Twigs of *E. robustum*                | Thongnest et al. (2013)                         |
|                              |    | Luteolin                                                                  | Aerial parts of *E. laurentii*         | Awouafack et al. (2018)                         |
|                              |    | Isosorentin or Luteolin-6-C-glucoside                                     | Aerial parts of *E. laurentii*         | Awouafack et al. (2018)                         |
|                              |    | 2′,O-a-L-Rhamnosyl-6-C-fucosyl-3′-O-methyl-luteolin                        | Aerial parts of *E. laurentii*         | Ateba et al. (2016a)                            |
| Flavonols                    |    | Kaempferol (*)                                                            | Roots of *E. chinense*                | Thongnest et al. (2013)                         |
|                              |    | Astragalin or Kaempferol-3-O-β-D-glucopyranoside (*)                      | Roots of *E. chinense*                | Thongnest et al. (2013)                         |
|                              |    | Quercetin (*)                                                             | Whole plant of *E. glomeratum*         | Thongnest et al. (2013)                         |
|                              |    | Quercetin-3-O-methyl ether                                                | Aerial parts of *E. laurentii*         | Ateba et al. (2014b)                            |
|                              |    | 3,4′,6,8-Tetrahydroxyflavone-7-C-glucoside                                | Aerial parts of *E. laurentii*         | Ateba et al. (2014b)                            |
|                              |    | Robustiflavone A or 2′,3′,5′,5,7-pentahydroxy-3,4′-dimethoxyflavone (*)   | Roots of *E. chinense*                | Thongnest et al. (2013)                         |
|                              |    | Robustiflavone B or 2′,3′,5′,5,7-pentahydroxy-4′-methoxyflavone (*)       | Roots of *E. chinense*                | Thongnest et al. (2013)                         |
|                              |    | Dehydrolupinifolinol (*)                                                  | Roots of *E. chinense*                | Sutthivayakit et al. (2009)                     |
|                              |    | Khonklonginol F or 3,5-dihydroxy-4′-methoxy-6′,6′-dimethylpyranono (2′,3′,7,6)-8-(3′,3′-dimethyallylfлаванone (') | Roots of *E. chinense*                | Sutthivayakit et al. (2009)                     |
| Flavanones or dihydroflavanols |    | 3,5′,2′-Tetrahydroxy-6′,6′-dimethylpyranono (2′,3′,7,6)-8-(3′,3′-dimethyallylfлаванone (') | Roots of *E. chinense*                | Thongnest et al. (2013)                         |
|                              |    | 3,4′,6,8-Tetrahydroxyflavone-7-C-glucoside                                | Aerial parts of *E. laurentii*         | Ateba et al. (2016a)                            |
|                              |    | (2S,3S)-6,8,3′-Triplyrenyl-dihydromorin or (2S,3S)-6,8,3′-triptyrenyl-3,5,7,2′,4′-pentahydroxyflavanone | Underground parts of *E. laurentii*    | Ateba et al. (2016b)                            |
|                              |    | Lupinifolinol (')                                                         | Roots of *E. chinense*                | Sutthivayakit et al. (2009), Thongnest et al. (2013) |
|                              |    | 3-epi-Lupinifolinol or (2R,3S)-3,5,4′-trihydroxy-6′,6′-dimethylpyranono (2′,3′,7,6)-8-(3′,3′-dimethyallylfлаваноне (') | Roots of *E. chinense*                | Thongnest et al. (2013)                         |
|                              |    | 2′-Hydroxylupinifolinol or (2R, 3R)-3,5,2′,4′-tetrahydroxy-6′,6′-dimethylpyranono (2′,3′,7,6)-8-(3′,3′-dimethyallylfлаваноне (') | Roots of *E. chinense*                | Thongnest et al. (2013)                         |
|                              |    | 3-epi-Khonklonginol C or (2R,3S)-3,5,2′,4′-trihydroxy-4′-methoxy-6′,6′-dimethylpyranono (2′,3′,7,6)-8-(3′,3′-dimethyallylfлаваноне (') | Roots of *E. chinense*                | Thongnest et al. (2013)                         |

(Continued on following page)
| Chemical classes | N° | Compounds | Plant parts and species | References |
|------------------|----|-----------|------------------------|------------|
|                  | 27. | Khonklonginol A or 3,5-dihydroxy-4′-methoxy-6′,6″-dimethylpyrano (2″,3″:7,6)-8-(3′″,3″″-dimethylallyl) flavanone (*)&nbsp; | Roots of *E. chinense* | Thongnest et al. (2013) |
|                  | 28. | Khonklonginol B or 3,5-dihydroxy-4′-methoxy-6′,6″-dimethylpyrano (2″,3″:7,6)-8-(3′″,3″″-dimethylallyl) flavanone (*)&nbsp; | Roots of *E. chinense* | Sutthivaiyakit et al. (2009) |
|                  | 29. | Khonklonginol C or 3,5,2′-trihydroxy-4′-methoxy-6″,6″-dimethylpyrano (2″,3″:7,6)-8-(3′″,3″″-dimethylallyl) flavanone (*)&nbsp; | Roots of *E. chinense* | Sutthivaiyakit et al. (2009) |
|                  | 30. | Khonklonginol D or 3,5-dihydroxy-3′,4′-dimethoxy-6″,6″-dimethylpyrano (2″, 3″: 7,6)-8-(3′″,3″″-dimethylallyl) flavanone (*)&nbsp; | Roots of *E. chinense* | Sutthivaiyakit et al. (2009) |
|                  | 31. | Khonklonginol E or 3,5-dihydroxy-3′,4′-dimethoxy-6″,6″-dimethylpyrano (2″,3″:7,6)-8-(3′″,3″″-dimethylallyl) flavanone (*)&nbsp; | Roots of *E. chinense* | Sutthivaiyakit et al. (2009) |
|                  | 32. | Khonklonginol F or 3,5-dihydroxy-4′-methoxy-6′,6″-dimethylpyrano (2″,3″:7,6)-8-(3′″,3″″-dimethylallyl) flavanone (*)&nbsp; | Roots of *E. chinense* | Sutthivaiyakit et al. (2009) |
|                  | 33. | Khonklonginol G or 5-hydroxy-4′-methoxy-6″,6″-dimethylpyrano (2″,3″:7,6)-8-(3′″,3″″-dimethylallyl) flavanone (*)&nbsp; | Roots of *E. chinense* | Sutthivaiyakit et al. (2009) |
| Flavonones       | 34. | Eriosemaone A (*) | Roots of *E. tuberosum* | Ma et al. (1995) |
|                  | 35. | Eriosemaone B (*) | Roots of *E. chinense* | Sutthivaiyakit et al. (2009) |
|                  | 36. | Eriosemaone C (*) | Roots of *E. tuberosum* | Ma et al. (1995) |
|                  | 37. | Khonklonginol H or 5′-hydroxy-4′-methoxy-6″,6″-dimethylpyrano (2″,3″:7,6)-8-(3′″,3″″-dimethylallyl) flavanone (*)&nbsp; | Roots of *E. chinense* | Sutthivaiyakit et al. (2009) |
|                  | 38. | Khonklonginol I or 5′-hydroxy-4′-methoxy-6″,6″-dimethylpyrano (2″,3″:7,6)-8-(3′″,3″″-dimethylallyl) flavanone (*)&nbsp; | Roots of *E. chinense* | Sutthivaiyakit et al. (2009) |
|                  | 39. | Lupinolin (*) | Roots of *E. tuberosum* | Ma et al. (1996) |
|                  | 40. | Flemichin D (*) | Roots of *E. tuberosum* | Prasad et al. (2013) |
|                  | 41. | 6-Prenyl pinocembrin (*) | Twigs of *E. robustum* | Awouafack et al. (2013) |
|                  | 42. | Prunin | Twigs of *E. robustum* | Awouafack et al. (2018) |

*Continued on following page*
### TABLE 3 (Continued)

Compounds isolated/identified from *Eriosema* species (the structure of compounds illustrated in Figure 2).

| Chemical classes | N° | Compounds                          | Plant parts and species                          | References |
|------------------|----|------------------------------------|-------------------------------------------------|------------|
| Isoflavones      | 43. | Genistein (*)                      | Roots and twigs of *E. tuberosum*                | Ma et al. (1998), Awouafack et al. (2018) |
|                  | 44. | 2′-Hydroxygenistein                | Roots of *E. chinense*                          | Thongnest et al. (2013) |
|                  | 45. | 5,7,4′-Trihydroxy-2′-methoxyisoflavone | Aerial and underground parts of *E. laurentii* | Ateba et al. (2013), Ateba et al. (2016b) |
|                  | 46. | 4′,5-Dihydroxy-2′,7-dimethoxyisoflavone | Aerial and underground parts of *E. laurentii* | Ateba et al. (2014b), Ateba et al. (2016b) |
|                  | 47. | Isoluteolin (*)                    | Roots of *E. psoraleoides*                      | Wanyama (2010) |
|                  | 48. | 5-O-Methylgenistein (*)            | Roots of *E. psoraleoides*                      | Wanyama (2010) |
|                  | 49. | Tectorigenin (*)                   | Whole plant of *E. glomeratum*                  | Ateba et al. (2013), Ateba et al. (2016b) |
|                  | 50. | 7-O-Methyltectorigenin (*)         | Whole plant of *E. glomeratum*                  | Ateba et al. (2013), Ateba et al. (2016b) |
|                  | 51. | 5,7,2′,4′-Tetrahydroxy-6-methoxyisoflavone (*) | Whole plant of *E. glomeratum*                  | Ateba et al. (2013), Ateba et al. (2016b) |
|                  | 52. | 4′,7′-Bisgenistein                 | Whole plant of *E. glomeratum*                  | Ateba et al. (2013), Ateba et al. (2016b) |
|                  | 53. | 8,5-O-Genistein-7-O-β-D-glucopyranoside (*) | Whole plant of *E. glomeratum*                  | Ateba et al. (2013), Ateba et al. (2016b) |
|                  | 54. | Genistein or genistein-7-O-β-D-glucopyranoside (*) | Whole plant of *E. glomeratum*                  | Ateba et al. (2013), Ateba et al. (2016b) |
|                  | 56. | 5-O-Methylgenistein-7-O-β-D-glucopyranoside (*) | Whole plant of *E. glomeratum*                  | Ateba et al. (2013), Ateba et al. (2016b) |
|                  | 57. | Eriosemaside C or 5-O-Methylgenistein-7-O-β-D-apiofuranosyl-(1→2)-O-β-D-glucopyranoside (*) | Whole plant of *E. glomeratum*                  | Ateba et al. (2013), Ateba et al. (2016b) |
|                  | 58. | Genistein-7-O-β-apiofuranosyl-(1→6)-O-β-D-glucopyranoside (*) | Whole plant of *E. glomeratum*                  | Ateba et al. (2013), Ateba et al. (2016b) |
|                  | 59. | 5-O-Methylgenistein-7-O-β-apiofuranosyl-(1→6)-O-β-D-glucopyranoside (*) | Whole plant of *E. glomeratum*                  | Ateba et al. (2013), Ateba et al. (2016b) |
|                  | 60. | Sphaerobioside (*)                 | Whole plant of *E. glomeratum*                  | Ateba et al. (2013), Ateba et al. (2016b) |
|                  | 61. | 2′-Hydroxygenistein-7-O-glucopyranoside | Whole plant of *E. glomeratum*                  | Ateba et al. (2013), Ateba et al. (2016b) |
|                  | 62. | Eriosemaone D or 5,7,2′-trihydroxy-6″,6″-dimethylpyran (2″,3″,4″,5″) isoflavone (*) | Whole plant of *E. glomeratum*                  | Ateba et al. (2013), Ateba et al. (2016b) |
|                  | 63. | 2′-O-Methyl-eriosemaone D or 5,7-dihydroxy-2′-methoxy-6″,6″-dimethyl-pyrano (2″,3″,4″,5″) isoflavone | Whole plant of *E. glomeratum*                  | Ateba et al. (2013), Ateba et al. (2016b) |
|                  | 64. | Kraussianone 1 or 5,2′-dihydroxy-[8″,6″-dimethylpyran (2″,3″,4″,5″)] [8″,6″-dimethylpyran (2″,3″,4″,5″)] isoflavone | Whole plant of *E. glomeratum*                  | Ateba et al. (2013), Ateba et al. (2016b) |
|                  | 65. | Kraussianone 2 (*)                 | Rootstock of *E. kraussianum*                   | Drewes et al. (2002) |
|                  | 66. | Kraussianone 3 (*)                 | Rootstock of *E. kraussianum*                   | Drewes et al. (2002) |
|                  | 67. | Kraussianone 4 (*)                 | Rootstock of *E. kraussianum*                   | Drewes et al. (2002) |
|                  | 68. | Kraussianone 5 (*)                 | Rootstock of *E. kraussianum*                   | Drewes et al. (2002) |
|                  | 69. | Kraussianone 6 (*)                 | Rootstock of *E. kraussianum*                   | Drewes et al. (2004) |
|                  | 70. | Kraussianone 7 (*)                 | Rootstock of *E. kraussianum*                   | Drewes et al. (2004) |

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### TABLE 3 (Continued) Compounds isolated/identified from Eriosema species (the structure of compounds illustrated in Figure 2).

| Chemical classes | N° | Compounds | Plant parts and species | References |
|------------------|----|-----------|-------------------------|------------|
| Isoflavanones    | 71 | Cajanol (*) | Roots of *E. chinense* | Thongnest et al. (2013) |
| Coumaronochromones | 72 | Eriocoumaronochromone | Twigs of *E. robustum* | Awouafack et al. (2018) |
|                  | 73 | Lupinalbin A or 5,7,4′-trihydroxycoumaronochromone | Aerial and underground parts of *E. laurentii* | Ateba et al. (2014b), Ateba et al. (2016b) |
|                  | 74 | Desmoxyphyllin A or 5,7,4′-trihydroxy-5′-methoxycoumaronochromone | Twigs of *E. robustum* | Awouafack et al. (2018) |
| Chromones        | 75 | Eriosematin or 5-hydroxy-8-γ,γ-dimethylallyl-6′,6″-dimethylpyrano (3″,2″:6,7) chromone | Roots of *E. tuberosum* | Ma et al. (1995) |
|                  | 76 | Iso-eriosematin or 5-hydroxy-6-γ,γ-dimethylallyl-6′,6″-dimethyl-pyrano (2′, 3′: 7,8) chromone | Roots of *E. tuberosum* | Ma et al. (1996a) |
|                  | 77 | Eriosematin A or 5,7-dihydroxy-8-γ,γ-dimethylallyl chromone | Roots of *E. tuberosum* | Ma et al. (1996a) |
|                  | 78 | Eriosematin B or 5,7-dihydroxy-6-(3-hydroxy-3,3-dimethylbutyl)-8-γ,γ-dimethylallyl chromone | Roots of *E. tuberosum* | Ma et al. (1996a) |
|                  | 79 | Eriosematin C or 5,7-dihydroxy-8-γ,γ-dimethylallyl-8-γ,γ-dimethylallyl chromone | Roots of *E. tuberosum* | Ma et al. (1996a) |
|                  | 80 | Eriosematin D or 2,5-dihydroxy-6-γ,γ-dimethylallyl-6′,6″-dimethylpyrano (2′,3′:7,8) chromone | Roots of *E. tuberosum* | Ma et al. (1996b) |
|                  | 81 | Eriosematin E or 2,5-dihydroxy-8-γ,γ-dimethylallyl-6″-dimethylchromone-7-O-rutinoside | Roots of *E. chinense* | Prasad et al. (2017) |
|                  | 82 | Eriosemaside A or 5,7-dihydroxy-8-γ,γ-dimethylallylchromone-7-O-rutinoside | Roots of *E. tuberosum* | Ma et al. (1999) |
| Lignans          | 83 | Syringaresinol | Aerial parts of *E. laurentii* | Ateba et al. (2016a) |
|                  | 84 | Yangambin | Roots of *E. chinense* | Sutthivaiyakit et al. (2009) |
| Terpenoids       | 85 | Olean-12- ene-3,16,23-triol | Whole plant of *E. glomeratum* | Awouafack et al. (2008) |
| Sterols          | 86 | β-Stigmasterol | Twigs of *E. robustum* | Awouafack et al. (2013a) |
|                  | 87 | Stigmasterol | Roots of *E. chinense* | Thongnest et al. (2013) |
|                  | 88 | β-Stigmasterol-3-O-β-D-glucopyranoside | Twigs of *E. robustum* | Awouafack et al. (2013a), Thongnest et al. (2013) |
| Sesquiterpenes   | 89 | Clovanediol | Roots of *E. chinense* | Thongnest et al. (2013) |
| Monoterpenes     | 90 | Caryolane-1,9-diol | Roots of *E. chinense* | Thongnest et al. (2013) |
|                  | 91 | Ascaridole | Leaves of *E. englerianum* | Mbengwa et al. (2009) |
|                  | 92 | Terpinolene | Leaves of *E. englerianum* | Mbengwa et al. (2009) |

(Continued on following page)
TABLE 3 | (Continued) Compounds isolated/identified from *Eriosema* species (the structure of compounds illustrated in Figure 2).

| Chemical classes                     | N*       | Compounds                                                                 | Plant parts and species                      | References                     |
|--------------------------------------|----------|--------------------------------------------------------------------------|----------------------------------------------|---------------------------------
| **Toluene derivatives**              | 93       | O-Cymene                                                                 | Leaves of *E. englerianum*                   | Mmbengwa et al. (2009)          |
| **Benzoic acid Derivatives**         | 94       | 4-Hydroxybenzoic acid or p-Hydroxybenzoic acid                          | Roots of *E. tuberosum*                     | Ma et al. (1999)                |
|                                      | 95       | 3,4-Dihydroxybenzoic acid                                               | Aerial parts of *E. laurentii*               | Ateba et al. (2016a)            |
|                                      | 96       | Vanillic acid                                                           | Roots of *E. tuberosum*                     | Ma et al. (1999)                |
|                                      | 97       | 2,6-Dihydroxybenzoic acid                                               | Aerial parts of *E. laurentii*               | Ateba et al. (2016a)            |
|                                      | 98       | Eriosematin F or 3,4 dihydro-4-methoxy-naphthalene-2-carboxylic acid    | Roots of *E. tuberosum*                     | Ma et al. (1999)                |
| **Fatty acids**                      | 99       | Eicosanoic acid or arachidic acid                                       | Twigs of *E. robustum*                      | Awouafack et al. (2013a)       |
|                                      | 100      | Tetratriacontanoic acid                                                 | Whole plant of *E. glomeratum*              | Awouafack et al. (2008)        |
| **Glycerol derivative**              | 101      | 1-O-Heptatriacontanoyl glycerol                                         | Twigs of *E. robustum*                      | Awouafack et al. (2013a)       |
| **Coumarate**                        | 102      | Octaeicosanyl-trans-p-coumarate                                         | Roots of *E. chinense*                      | Thongnest et al. (2013)        |
| **Fatty alcohol**                    | 103      | Triacontanol                                                            | Whole plant of *E. glomeratum*              | Awouafack et al. (2008)        |
| **Phenols**                          | 104      | Hydroquinone                                                            | Roots of *E. tuberosum*                     | Ma et al. (1999)                |
|                                      | 105      | Arbutin                                                                  | Roots of *E. tuberosum*                     | Ma et al. (1999)                |
|                                      | 106      | Eriosemaside B or 4-hydroxyphenyl β-o-apiofuranosyl-(1→2)-O-β-c-glucopyranoside | Roots of *E. tuberosum*                     | Ma et al. (1999)                |
| **Cerebroside**                      | 107      | Orostachyscerebroside A                                                 | Twigs of *E. robustum*                      | Awouafack et al. (2013a)       |

*Flavonoids compiled by Awouafack et al. (2015).*
FIGURE 2 | Structures of dihydrochalcones (1–2), flavones (3–9), flavonols (10–20), dihydroflavonols (22–33), isoflavonones (34–42), isoflavones (43–70), isoflavonones (71), coumaronochromones (72–74), chromones (75–82), lignans (83–84), terpenoids (85–92) and other compounds (93–107) from *Eriosema* spp.
respectively, were also identified for the first time in the genus. Among flavanones, prunin (42) was isolated from the twigs of *E. robustum* (Awouafack et al., 2018).

The isoflavones, genistein (43), 2′-hydroxygenistein (44), genistin (54), genistein-8-C-glicoside (55), 2′-hydroxygenistein-7-O-glicoside (61), erosemaone D (62) and the new compound
2′-O-methyl-eriosemaone D (63) were identified and/or isolated from *E. laurentii* (Ateba et al., 2013; 2014b; 2016a; 2016b). Compound 43 was also obtained from the EtOAc-soluble portion of an EtOH extract of the twigs of *E. robustum* (Awouafack et al., 2018). 5,7,4′-trihydroxy-2′-methoxyisoflavone (45), 4′,5-dihydroxy-2′,7-
dimethoxyisoflavone (46) and 4',7''-bisgenistein (53) were obtained from a dichloromethane/methanol (1:1 v/v) root extract of *E. psoraleoides* (Wanyama, 2010). The coumaronochromone named eriocoumaronochromone (72) was isolated for the first time from an EtOH extract of the twigs of *E. robustum*, along with desmoxyphyllin A (74) (Awouafack et al., 2018). Lupinalbin A (73) was proven in methanol extracts of the aerial and underground parts of *E. laurentii* (Ateba et al., 2014b; 2016b) and in a dichloromethane/methanol (1:1 v/v) root extract of *E. psoraleoides* (Wanyama, 2010).

Chromones

All chromones known in the genus including eriosematin (75), iso-eriosematin (76), eriosematin A-E (77–81) and eriosemaside A (82) were obtained from the roots of *E. tuberosum* (Ma et al., 1995; 1996a; 1996b, 1999). Compound 81 was also identified in an ethanol root extract of *E. chinense* (Prasad et al., 2017).

Lignans

Syringaresinol (83) was isolated from the aerial parts of *E. laurentii* (Ateba et al., 2016a), while yangambin (84) was found in the roots of *E. chinense* (Sutthivaiyakit et al., 2009).

Terpenoids

The investigation of a dichloromethane/methanol (1:1, v/v) extract of the whole plant of *E. glomeratum* gave the triterpenoid olean-12-ene-3,16,23-triol (85) and the sterol 3-O-β-D-sitosterol glucopyranoside (88) (Awouafack et al., 2008). The sterols β-sitosterol (86) and stigmasterol (87) were reported from an ethanol extract of the twigs of *E. robustum* (Awouafack et al., 2013a) and roots of *E. chinense* (Thongnest et al., 2013). The sesquiterpenes clovandiol (89) and caryolane-1,9-diol (90) were obtained from roots of *E. chinense* (Thongnest et al., 2013), while the monoterpenes ascaridole (91) and terpinolene (92) have been isolated from the essential oil of leaves of *E. englerianum* (Mmbengwa et al., 2009).

Other Compounds

O-cymene (93) was obtained as a major phytoconstituent of the essential oil from fresh leaves of *E. englerianum*. 4-Hydroxybenzoic acid (94) was isolated from roots of *E. tuberosum* (Ma et al., 1999) and twigs of *E. robustum* (Awouafack et al., 2018) and from the aerial parts of *E. laurentii* along with 3,4-dihydroxybenzoic acid (95) and 2,6-dihydroxybenzoic acid (97) (Ateba et al., 2016a). Vanillic acid (96) and eriosematin F (98) were found in roots of *E. tuberosum* (Ma et al., 1999). Eicosanoic acid (99) was isolated from twigs of *E. robustum* (Awouafack et al., 2013a) and tetratriacontanoic acid (100) from a whole plant extract of *E. glomeratum* (Awouafack et al., 2008). The glycerol derivative 1-O-heptatriacontanoyl glycerol (101) was isolated from roots of *E. chinense* (Thongnest et al., 2013), while octaeicosanyl-trans-p-coumarate (102) was obtained from the roots of *E. chinense*.
The fatty alcohol triacontanol (103) was isolated from *E. glomeratum*. Three phenols identified as hydroquinone (104), arbutin (105) and eriosemaside B (106) were isolated from the roots of *E. tuberosum* (Ma et al., 1999). Twigs of *E. robustum* contained orostachyscerebroside A (107) (Awouafack et al., 2013a).

Globally the phytochemical investigation of the *Eriosema* genus led to the isolation and/or identification of 107 compounds from only eight species (5.3% of the genus) out of ca. 150 (*E. chinense*, *E. englerianum*, *E. glomeratum*, *E. kraussianum*, *E. laurentii*, *E. robustum*, *E. tuberosum* and *E. psoraleoides*). Isolated and/or identified constituents are mostly isoflavones (26.2%), flavonols (11.2%), flavanones (11.2%), flavanones (8.4%) and chromones (7.5%) (Figure 3). Awouafack et al. (2015) documented flavonoids from 5 *Eriosema* species and concluded that the genus represents a rich source of flavonoids, mostly isoflavones which could be considered as markers for the genus and have chemotaxonomic significance. However, given the low number of species investigated until now, the deduction of a chemotaxonomic significance of some of the components seems premature.

**PHARMACOLOGY**

Based on their ethnopharmacological use, *Eriosema* species aroused the interest of the scientific community. In line with this, many studies have been carried out aiming at evaluating or confirming the therapeutic potential of species from this genus. As depicted in Table 4, extracts and constituents from *Eriosema* species are shown to be responsible for a wide range of pharmacological activities such as aphrodisiac, anti-diarrheal, anti-oxidant, anti-microbial, anti-diabetic/hypoglycemic and estrogenic properties.

**Anticancer Activities**

The *in vitro* antiproliferative or cytotoxic activity of extracts and compounds from *E. chinense*, *E. robustum* and *E. griseum* against various cancer cell lines has been reported suggesting some preliminary potential for cancer treatment. Using the MTT (3-(4,5-dimethylthiazolyl-2)-2,5-diphenyltetrazolium bromide) cell viability assay, a hexane root extract of *E. chinense* exhibited a moderate cytotoxic activity against human small-cell lung (NCI-H187) (IC$_{50}$ of 12.0 μg/ml) and oral epidermal carcinoma (KB) (IC$_{50}$ of 9.9 μg/ml) cells. Normal monkey kidney Vero cells were also moderately (IC$_{50}$: 5.8 μg/ml) affected (Sutthivaiyakit et al., 2009). Khonklonginols A (27), F (19) and H (38), lupinifolinol (23), dehydrolupinifolinol (18) and flemichin D (40) from the roots of *E. chinense* exhibited a strong cytotoxicity (IC$_{50}$ of 2.4–3.9 μg/ml) toward NCI-H187 cells while khonklonginol B (28), lupinifolin (39) and eriosemaone A (34) with IC$_{50}$ values of 4.3, 6.5 and 6.0 μg/ml, respectively, were moderately cytotoxic (Sutthivaiyakit et al., 2009). Toward KB cells, compounds 23, 27, 28, 39 and 40 displayed a strong cytotoxic effect, while 18, 19, 34 and 38 showed a moderate effect. Compounds 18, 19, 27 and 38 displayed a significant cytotoxicity (IC$_{50}$ of 6.4–11.1 μg/ml) toward Vero cells.

**Antioxidant Activities**

By controlling the formation and scavenging of reactive oxygen and nitrogen species (ROS/RNS) as well as interrupting the related chain reactions and lipid peroxidation, antioxidants constitute the first line of defense against the genesis of various chronic and degenerative diseases. Different *in vitro* methodologies, including the DPPH (1,1-di-phenyl-2-
TABLE 4 | Pharmacological properties of *Eriosema* spp.

| Pharmacological activities | *Eriosema* species | Parts/extracts | Model | Dosage/concentration and route of administration in the animal studies | Results | References |
|-----------------------------|-------------------|----------------|-------|-----------------------------------------------------------------|---------|------------|
| Anticancer                  | *E. chinense*     | Roots/hexane extract | *In vitro*: MTT assay Small-cell lung (NCl-H187), oral epidermal carcinoma (K2) human cancer cells | Moderate activity (IC50:12.0 μg/ml) against small-cell lung and oral epidermal carcinoma (IC50: 9.9 μg/ml) human cells | Sutthivaiyakir et al. (2009) |
| Anti-oxidant                | *E. englerianum*  | Leaves/essential oil | *In vitro*: β-carotene bleaching assay | Color retention zone of 14.4 mm | Mnbiengwa et al. (2009) |
|                            | *E. chinense*     | Roots/EtOH extract | *In vitro*: PFRAP assay | Reducing power of 0.263 μg/ml | Prasad et al. (2013b) |
|                            |                   |                 | *In vitro*: DPPH, H2O2 and nitric oxide radical scavenging assays | Scavenging activities of differing degree with IC50 values of 146, 221, 233 and 170 μg/ml, respectively | |
|                            | *E. robustum*     | Twigs/EtOH extract | DPPH assay | Scavenging activity with IC50 ≥ 1.13 mg/ml | Awouafack et al. (2013b) |
| Estrogenic                  | *E. laurentii*    | Aerial parts/MeOH extract | *In vitro*: ERα yeast two-hybrid assay | 1–83 μg/ml | Concentration-dependent β-galactosidase activity | Ateba et al. (2013) |
|                            |                   |                 | *In vivo*: Ovariectomized Wistar rats | 50, 100 and 200 mg/kg daily for 3 days and 9 weeks p.o | Vaginal stratification and cornification, no effect on uterus | Ateba et al. (2013) |
|                            |                   | Underground parts/MeOH extract | *In vivo*: Ovariectomized Wistar rats | 50, 100 and 200 mg/kg daily for 3 days p.o | No effect on uterus and vagina | Ateba (2014c) |
| Aryl hydrocarbon agonistic  | *E. laurentii*    | Aerial parts/MeOH extract | *In vitro*: AhR yeast β-galactosidase assay | 1–83 μg/ml | Concentration-dependent AhR β-galactosidase activity | Ateba et al. (2013) |
|                            |                   | Underground parts/MeOH extract | | 1–125 μg/ml | | Ateba et al. (2016b) |
| Anti-osteoporosis           | *E. laurentii*    | Aerial parts/MeOH extract | *In vivo*: Ovariectomized Wistar rats | 50, 100 and 200 mg/kg daily for 9 weeks p.o | ↑ dry femur weight, ↑ serum and femur calcium levels | Ateba et al. (2013) |
|                            |                   |                 | | | ↓ serum inorganic phosphorus levels, ↓ femur inorganic phosphorus levels | |
|                            |                   |                 | | | ↓ Fasting blood glucose levels in dose-dependent manner from 2 to 8 h after treatment with peak effects 4 h after | Ojewole et al. (2007) |
|                            |                   |                 | | | ↓ Fasting blood glucose levels from day 6 | Nduka et al. (2018), Nduka et al. (2019) |
|                            |                   |                 | | | ↓ Fasting blood glucose levels from day 2–7 | Elechi et al. (2019) |
| Hypoglycemic and anti-diabetic | *E. krusiasmum* | Rootstock/hydro-alcoholic extract | *In vivo*: normal Wistar and streptozotocin-induced diabetic Wistar rats | 40, 80, 160 and 320 mg/kg p.o. (single dose) | ↓ Fasting blood glucose levels in dose-dependent manner from 2 to 8 h after treatment with peak effects 4 h after | Ojewole et al. (2007) |
|                            | *E. psoraleoides* | Leaves/H2O and EtOH extracts | *In vivo*: aloxan-induced diabetic Wistar rats 200 and 400 mg/kg daily for 7 days p.o | | ↓ Fasting blood glucose levels from day 2–7 | Elechi et al. (2019) |
|                            |                   | Leaves/n-hexane extract, n-hexane-DCM and DCM fractions | *In vivo*: aloxan-induced diabetic Wistar rats 200 mg/kg daily for 7 days p.o | | | |
| Cardiovascular protection   | *E. laurentii*    | Aerial parts/MeOH extract | *In vivo*: postmenopause-like model (ovariectomized Wistar rats) | 50, 100 and 200 mg/kg daily for 9 weeks p.o | ↓ total cholesterol (TC) and LDL levels | Ateba et al. (2013) |
|                            |                   |                 | | | ↑ HDL | |
|                            |                   |                 | | | ↓ TC/HDL and LDL/HDL ratios, atherogenic plasma index | Ndhla et al. (2011) |
| Acetylcholinesterase inhibition | *E. cordatum* | Roots/H2O extract | *In vitro*: Acetylcholinesterase inhibition | | | |

(Continued on following page)
| Pharmacological activities | Eriosema species | Parts/extracts | Model | Dosage/concentration and route of administration in the animal studies | Results | References |
|---------------------------|------------------|----------------|-------|------------------------------------------------------------------|---------|------------|
| Anti-microbial            | Eriosema campestre var. campestre | Leaves/MeOH extract | In vitro | Trichophyton rubrum, Trichophyton mentagrophytes, Microsporum gypseum, Epidermophyton floccosum, Candida albicans ATCC 90028, Candida kru sei ATCC 6258, Candida glabrata HCGL01, Candida tropicalis ATCC 750, Candida parapsilosis ATCC22019 | 500 μg/ml | Fungistatic toward T. rubrum, T. mentagrophytes and E. floccosum. Inactive against M. gypseum and all tested Candida strains | de Morais et al. (2017) |
|                           | Eriosema campestre var. macrophyllum | Leaf/MeOH extract | In vitro | Trichophyton rubrum, Trichophyton mentagrophytes, Microsporum gypseum, Epidermophyton floccosum, Candida albicans ATCC 90028, Candida kru sei ATCC 6258, Candida glabrata HCGL01, Candida tropicalis ATCC 750, Candida parapsilosis ATCC22019 | 500 μg/ml | Fungistatic toward T. mentagrophytes and E. floccosum. Inactive against T. rubrum, M. gypseum and all tested Candida strains | de Morais et al. (2017) |
|                           | E. cordatum       | Roots/petroleum ether, DCM, EtOH and H₂O extracts | In vitro | Staphylococcus aureus, Bacillus subtilis, Escherichia coli, Klebsiella pneumonia | MIC of 390 μg/ml with ethanolic extract, MIC of 195 μg/ml against S. aureus and B. subtilis, and of 390 μg/ml against E. coli and K. pneumoniae with dichloromethane extract, Petroleum ether and H₂O extracts not active | Ndhlala et al. (2011) |
|                           | E. chinense       | Roots/EtOH extract | In vitro | Escherichia coli ATCC25922, Shigella flexneri ATCC12022, Pseudomonas aeruginosa ATCC27893, Staphylococcus aureus ATCC25323, Salmonella typhi, Shigella dysenteriae, Proteus vulgaris, Klebsiella pneumoniae, Shigella boydii, Bacillus cereus, Enterococcus faecalis | MICs >195 μg/ml | | Prasad et al. (2013) |

(Continued on following page)
### TABLE 4 | (Continued) Pharmacological properties of Eriosema spp.

| Pharmacological activities | Eriosema species | Parts/extracts | Model | Dosage/concentration and route of administration in the animal studies | Results | References |
|---------------------------|------------------|----------------|-------|---------------------------------------------------------------------|---------|------------|
|                           | *E. engleriannum* | Leaves/essential oil | *In vitro* | Staphylococcus aureus, Escherichia coli, Pseudomonas aeruginosa, Bacillus subtilis, Klebsiella pneumoniae, Proteus vulgaris, Clostridium sporogenes, Acinetobacter calcoaceticus, Candida albicans, Aspergillus niger, Aspergillus flavus | 1, 2, 5 and 10 μl/ml IZ ≥ 7 mm at 5 μl/ml (A. calcoaceticus) and 10 μl/ml (C. sporogenes and A. calcoaceticus) ↓ growth of C. albicans (24.2–42.6%), Aspergillus niger (34.7–49.7%) and Aspergillus flavus (27.5–39.3%) | Mmbengwa et al. (2009) |
|                           | *E. glabrum*     | Leaves/MeOH extract | *In vitro* | Trichophyton rubrum, Trichophyton mentagrophytes, Microsporum gypseum, Epidermophyton floccosum, Candida albicans ATCC 90028, Candida kruisel ATCC 6258, Candida glabrata HCCGL01, Candida tropicalis ATCC 750, Candida parapsilosis ATCC22019 | 500 μg/ml | Fungicidal toward T. mentagrophytes and E. floccosum, Inactive against T. rubrum, M. gypseum and all tested Candida strains | de Morais et al. (2017) |
|                           | *E. glomeratum*  | Stem and leaves/MeOH-DCM extract | *In vitro* | Staphylococcus aureus ATCC25923, Klebsiella pneumonia ATCC13883, Moresella catarrhalis ATCC 14468, Mycobacterium smegmatis ATCC23246, Mycobacterium aurum NCTC10437 | Stem extract: MICs of 500, 1000, 1000, 65, and 50 μg/ml, respectively Leaf extract: MICs of 1,000, 500, 1,000,130 and 1,000 μg/ml, respectively | | Formone-Fodjo et al. (2014) |
|                           | *E. heterophyllum* | Leaves/MeOH extract | *In vitro* | Trichophyton rubrum, Trichophyton mentagrophytes, Microsporum gypseum, Epidermophyton floccosum, Candida albicans ATCC 90028, Candida kruisel ATCC 6258, Candida glabrata HCCGL01, Candida tropicalis ATCC 750, Candida parapsilosis ATCC22019 | 500 μg/ml | Fungistatic toward T. rubrum, T. mentagrophytes and M. gypseum. Fungicidal against E. floccosum, Inactive against, and all tested Candida strains | de Morais et al. (2017) |
### TABLE 4 (Continued) Pharmacological properties of Eriosema spp.

| Pharmacological activities | Eriosema species | Parts/extracts | Model | Dosage/concentration and route of administration in the animal studies | Results | References |
|----------------------------|-----------------|----------------|-------|-------------------------------------------------|---------|------------|
|                            | Eriosema longifolium | Leaves/MeOH extract | In vitro | Trichophyton rubrum, Trichophyton mentagrophytes, Microsporum gypseum, Epidermophyton floccosum, Candida albicans ATCC 90028, Candida krusei ATCC 6258, Candida glabrata HCCGL01, Candida tropicalis ATCC 750, Candida parapsilosis ATCC22019 | 500 μg/ml | Inactive | de Morais et al. (2017) |
|                            | E. montanum    | Leaves/polar fraction of an EtOH extract | In vitro | Bacillus cereus ATCC 14579, Enterobacter cloacae ATCC 13047, Escherichia coli ATCC 8739, Klebsiella pneumoniae ATCC 13883, Mycobacterium fortuitum ATCC 6841, Proteus vulgaris ATCC 13315, Pseudomonas aeruginosa ATCC 15442, Salmonella typhimurium ATCC 13311, Staphylococcus aureus ATCC 6538, Streptococcus pyogenes ATCC 12344, Candida albicans ATCC 10231, Trichophyton rubrum RV 58125, Epidermophyton floccosum RV 71625, Microsporum canis RV 66973 | MIC > 750 μg/ml | | Cos et al. (2002b) |
|                            | E. psoraleoides | Bark and wood of twigs/MeOH extract | In vitro | Streptococcus mutans HG982, Actinomyces viscosus HG485, Candida albicans HG392 | | | Khan et al. (2000) |
|                            |                | Stem bark/MeOH extract | In vitro | Candida albicans | | | Runyoro et al. (2006) |
|                            |                | Leaves/MeOH extract and its n-hexane and ethyl acetate fractions | In vitro | Escherichia coli ATCC35219, Staphylococcus aureus ATCC25923, Clinical isolates of Staphylococcus aureus, Proteus vulgaris, Klebsiella erogenes, Pseudomonas aeruginosa, Escherichia coli | | | Elechi and Igboh (2017) |

(Continued on following page)
### TABLE 4 | Pharmacological properties of Eriosema spp.

| Pharmacological activities | Eriosema species | Parts/extracts | Model | Dosage/concentration and route of administration in the animal studies | Results | References |
|----------------------------|------------------|----------------|-------|---------------------------------------------------------------------|---------|------------|
|                            | E. robustum      | Twigs/EtOH extract | In vitro | Staphylococcus aureus ATCC29213 Enterococcus faecalis ATCC29212 Pseudomonas aeruginosa ATCC27853 Escherichia coli ATCC25922 Candida albicans ATCC10231 Candida albicans Cryptococcus neoformans Aspergillus fumigatus | MIC of 80 μg/ml toward S. aureus E. faecalis and E. coli MIC of 310 μg/ml toward P. aeruginosa MIC of 160 μg/ml toward A. fumigatus MIC of 630 μg/ml against C. neoformans MIC of 1250 μg/ml toward C. albicans and C. albicans ATCC | Awouafack et al. (2013a) |
|                            | E. tacuaremboense | Leaves/MeOH extract | In vitro | Trichophyton rubrum Trichophyton mentagrophytes Microsporum gypseum Epidermophyton floccosum Candida albicans ATCC 90028 Candida kru sei ATCC 6258 Candida glabrata HCOCL01 Candida tropicalis ATCC 750 Candida parapsilosis ATCC22019 | 500 μg/ml | Fungistatic toward E. floccosum Inactive against T. rubrum, T. mentagrophytes, M. gypseum and all tested Candida strains | de Morais et al. (2017) |
| Anti-viral                 | E. montanum      | Leaves/polar fraction of an EtOH extract | In vitro | Human immunodeficiency virus type-1 infected MT-4 cells | Inactive (EC₅₀ > 166 μg/ml) | Cos et al. (2002a) |
|                            |                  |                |       | Herpes simplex virus type 1 and semiliki forest virus A7 Poliovirus type 1 strain 1A/S3 Coxackie B2 virus Coxsackie A6 virus enterovirus EV71 | 375 μg/ml | RF of 1⁰⁴ | Cos et al. (2002b) |
|                            |                  |                |       | Poliovirus type 1 strain 1A/S3 Coxackie B2 virus Coxsackie A6 virus enterovirus EV71 | 375 μg/ml | RF of 1⁰² | Cos et al. (2002b) |
| Anti-diarrheal             | E. chinense      | Roots/EtOH extract and its chloroform fraction | In vivo: normal rats | Extract: 400 mg/kg p.o Fraction: 100 mg/kg p.o | ↓ normal fecal excretion rate and water content Delayed onset of diarrhea ↓ mean defeication, peristaltic index, intestinal fluid volume, prostaglandine E₂-induced enteropooling Significant recovery of Na⁺ and K⁺ levels Prevention of alterations of nitric oxide, TBARS, SOD and catalase activities | Prasad et al. (2013c) |
|                            |                  |                |       | In vivo: enteropathogenic Escherichia coli-induced diarrhea | Extract: 100 and 200 mg/kg p.o Fraction: 50 and 100 mg/kg p.o | ↓ total number of stools, total number of diarrheal stools, weight of stools, mean defeication rate and water content ↓ Na⁺/K⁺-atpase activity, ↓ intestinal secretion | Parmar et al. (2019a) |

(Continued on following page)
| Pharmacological activities | Eriosema species | Parts/extracts | Model | Dosage/concentration and route of administration in the animal studies | Results | References |
|---------------------------|------------------|----------------|-------|-----------------------------------------------------------------|---------|------------|
| Anti-inflammatory          | *E. campestre*   | Roots/DCM-EtOH extract | *In vitro*: Peripheral blood mononuclear cells | 6.25, 12.5 and 25 μg/ml | ↓ T lymphocytes, including CD4+ and CD8+ cells. ↓ IL-2 levels in the supernatant of the cell cultures. | Santos et al. (2016) |
|                           | *E. cordatum*    | Roots/petroleum ether, DCM, EtOH and H2O extracts | *In vitro*: Cyclooxygenase inhibition | 250 μg/ml for organic extracts, 2 mg/ml for the aqueous extract | Inhibition of COX-1 activity by 13–34%. Inhibition of COX-2 activity by 6–35%. | Ndhlala et al. (2011) |
| Anthelmintic              | *E. griseum*     | Leaves/EtOH extract | *In vitro*: *Echinostoma caproni*, *Schistosoma mansoni*, *Ancylostoma ceylanicum*, *Heligmosomoides bakeri* and *Trichuris muris* | MLC of 20 μg/ml against third-stage larvae of *H. bakeri* and *S. mansoni* schizonts. MLC of 40 μg/ml against adult *S. mansoni*. Moderate activity against third-stage larvae of *A. ceylanicum*. No activity on adult *E. caproni* and *T. muris*. | 49.5% reduction of worm burden against adult *S. mansoni* at 400 mg/kg, No activity against *E. caproni* and *T. muris* at 800 and 400 mg/kg, respectively. | Koné et al. (2012) |
|                           |                  |                | *In vivo*: mice harboring adult *S. mansoni*, *E. caproni* and *T. muris* | Single oral dose of 400 or 800 mg/kg 49 days post-infection | 94.5% reduction of worm burden against adult *S. mansoni* at 400 mg/kg, No activity against *E. caproni* and *T. muris* at 800 and 400 mg/kg, respectively. | |

*↓*: decrease or inhibition; ↑: increase; DPPH (1,1-di-phenyl-2-picrylhydrazyl); DCM: dichloromethane; PFRAP: potassium ferricyanide antioxidant power, IC50: concentration of a substance required for 50% of its maximal inhibitory effect, IZ: diameter of inhibition zone, MIC: minimum inhibitory concentration, MLC: minimum lethal concentration, p. o.: per os, RF: reduction factor of the viral titer, SOD: superoxide dismutase, TBARS: thiobarbituric acid reactive substances.
picrylhydrazyl), nitric oxide radical and H₂O₂ scavenging assays, potassium ferricyanide antioxidant power (PFRAP), hydroxyl radical antioxidant capacity (HORAC), thiobarbituric acid reactive substances (TBARS) and the β-carotene bleaching test were used to evaluate the radical scavenging and antioxidant potential of members of the *Eriosema* genus.

Using a β-carotene bleaching assay, essential oil from fresh leaves of *E. englerianum* containing 3.65% ascaridole (91), 7.86% terpinolene (92) and 88.50% *O*-cymene (93) showed anti-oxidative activity with a color retention zone of 14.4 mm (Mmbengwa et al., 2009).

In the study by Prasad et al. (2013b), an ethanolic root extract of *E. chinense* (EEC) displayed a total antioxidant capacity of 90.2 µg/ml ascorbic acid equivalents. The PFRAP of the extract and the standard ascorbic acid was 0.26 and 0.42 µg/ml, respectively. The IC₅₀ values of the extract for DPPH, hydroperoxide, nitric oxide and hydroxyl radical were 146.3, 221.0, 232.9 and 170.2 µg/ml, respectively, whereas those of the standards ascorbic acid (DPPH assay), rutin (H₂O₂ and nitric oxide) and butylated hydroxyanisole (hydroxyl) were 79.1, 82.9, 76.4 and 71.9 µg/ml, respectively. The antioxidant capacity of fractions (hexane, chloroform, ethyl acetate and aqueous) of EEC was also evaluated. A total antioxidant capacity of 76.0, 97.4, 89.5 and 44.6 µg/ml ascorbic acid equivalents, respectively, was determined. In contrast, very low DPPH (IC₅₀ 163.1–312.1 µg/ml), nitric oxide (IC₅₀ 2013.8–372.2 µg/ml) and H₂O₂ (IC₅₀ ≥ 187.7 µg/ml) radical scavenging activities as well as a low HORAC (IC₅₀ ≥ 154.4 µg/ml) were observed for these fractions (Prasad et al., 2013a). Thongnest et al. (2013) evaluated the antioxidant activity of 11 flavonoids from the roots of *E. chinense* using a DPPH method. The most pronounced effects, close to the standard butylated hydroxytoluene (IC₅₀ of 39 µM), were observed with compounds 10 (IC₅₀ of 28 µM) and 20 (IC₅₀ of 35 µM), while 11, 12, 23–25, 27, 33, 40 and 49 with IC₅₀ ≥ 252 µM, were inactive. In rats, a single oral pretreatment (30 min before castor oil challenge) with EEC (at 400 mg/kg), its chloroform fraction (at 100 mg/kg), and compounds 39 (10 mg/kg) and 81 (10 mg/kg) prevented the alterations of nitric oxide, TBARS (lipid peroxidation), superoxide dismutase and catalase activities in the castor oil-mediated diarrhea model (Prasad et al., 2013c; Prasad et al., 2017). Compound 81 (5 and 10 mg/kg) restored the oxidative status (nitric oxide level, SOD and CAT activities) in the enteropathogenic *Escherichia coli*-induced diarrhea rat model.

The anti-oxidant activity of an ethanol extract of twigs of *E. robustum*, its fractions and the isolated compounds 16 and 17, 41 and 101 resulted in unphysiological IC₅₀ values (≥1.13 mg/ml) using a DPPH method (Awouafack et al., 2013b). Using the same assay, compounds 5 and 72 displayed IC₅₀ values of 340.3 and 524.6 µM, respectively, while that of ascorbic acid was 35.9 µM (Awouafack et al., 2018).

The antioxidant capacity of *Eriosema* species was evaluated in *vitro* by different methods addressing different mechanisms of action. Each of them has its strengths and weaknesses (Bibi Sadeer et al., 2020). The plant extracts and products are mixtures of compounds that can display their antioxidant activity through different mechanisms. Therefore, to better estimate the overall antioxidant activity of a sample, at least two (or even all) of these assays must be combined. Tan and Lim (2015) recommended a mix of single electron transfer based (DPPH, ABTS, FRAP, TBARS) and hydrogen atom transfer based (ORAC, HORAC, TRAP, crocin and β-carotene bleaching) assays. Among the six *in vitro* studies recorded in this review, just two (Prasad et al., 2013a; Prasad et al., 2013b) met with this requirement, while the other ones only used β-carotene bleaching (Mmbengwa et al., 2009) or DPPH (Awouafack et al., 2013b; Thongnest et al., 2013; Awouafack et al., 2018) assays. *In vitro* models are known to be not always reproducible in respective *in vivo* assays. Therefore, *in vivo* studies are necessary for the confirmation of such effects. Interestingly, the weakly active ethanol root extract of *E. chinense*, its chloroform fraction and the inactive compound 39 using DPPH method, restored the alterations of nitric oxide, TBARS, superoxide dismutase and catalase activities in the castor oil-mediated diarrhea model in rats (Prasad et al., 2013c). Although data at this level seems to be naive and preliminary for any conclusion, they are indicator of the antioxidant potential of members of the *Eriosema* genus. However, more species need to be investigated in *vitro* and *in vivo*.

### Estrogenic and Aryl Hydrocarbon Agonistic Properties

Estrogens deficiency (natural or surgical) is associated with numerous health problems including urogenital atrophy, hot flushes, osteoporosis and increased risk of cardiovascular diseases (Calleja-Agius and Brincat, 2015; Nappi and Cucinella, 2020). Given the adverse outcomes associated with the long-term usage of the hormone replacement therapy e.g. increased risk of endometrial and breast cancer, stroke and pulmonary thromboembolism, phytoestrogens have gained and continue to receive great interest.

The estrogenic properties of *E. laurentii*, traditionally used against female infertility, gynecological and menopausal complaints have been evaluated *in vitro* and *in vivo*. *In vitro*, a methanol extract of the aerial parts (AEL), its fractions and the predominant secondary metabolites 43, 44 and 73 induced a significant and concentration-dependent β-galactosidase activity in the ERα yeast two-hybrid assay (yERα) (Ateba et al., 2013; Ateba et al., 2014b). At 25 µg/ml, AEL was as potent as 10 nM estradiol (Ateba et al., 2013). Compounds 43, 44 and 73 displayed EC₅₀ values of 0.32 µM, 6.1 µM and 21.4 nM, respectively, while that of 17β-estradiol (E₂) was 0.27 nM. All the three compounds were full ERα agonists as they displayed the maximal efficacy of E₂ although at much higher concentrations (Ateba et al., 2014b). A methanolic extract of the underground parts of *E. laurentii* (UEL) was also highly active in yERα (Ateba et al., 2016b). The concentration of 10 µg/ml was as potent as 0.5 nM E₂. However, compounds 22, 62 and 63 from this extract did not show any yERα activity (Ateba et al., 2016b).
In vivo, a 3-days uterotrophic assay and a 9-weeks oral treatment in ovariectomized adult rats were tested. AEL at the doses of 50, 100 and 200 mg/kg p. o. did not induce endometrium proliferation either in the 3-days or the 9-weeks treatment regiments, but induced vaginal stratification and cornification (Ateba et al., 2013). This tissue-dependent effect suggests that AEL could prevent vaginal dryness experienced by menopausal women, while not inducing the unwanted uterine proliferation. In the other hand, the decoction of aerial parts of E. laurentii had no significant effect on the uterine and vaginal endpoints at all tested doses following a 3-days uterotrophic assay (Ateba et al., 2014c).

Studies reported the repressive effects of aryl hydrocarbon receptor (AhR) agonists on ERa estrogen-sensitive cancer (endometrium and breast) cells (Tsuchiya et al., 2005; Okino et al., 2009; Marconetti et al., 2010; Labrecque et al., 2012). In line with this, the agonistic properties of AEL and compounds were evaluated. AEL exhibited a dose-dependent and significant AhR β-galactosidase activity from 5 µg/ml. The activity at 83 µg/ml was similar to that of 50 nM β-naphthoflavone (Ateba et al., 2013). For the first time, 44 (EC50 not determined) and 73 (EC50 of 1.34 µM) were found as partial agonists of AhR, whereas 43 was not active (Ateba et al., 2014b).

Classical, suitable and reproducible systems/models have been used to evaluate estrogenic and aryl hydrocarbon agonistic properties of E. laurentii in vitro (Jungbauer and Beck, 2002; Reiter et al., 2009) and in vivo (OECD, 2007; Mvondo et al., 2011). Accordingly, all data reported in this section demonstrated the potential of E. laurentii for managing various gynecological and menopausal complaints. However, this species is also traditionally used for treating female infertility. Studies in that domain are needed. Similarly, a wide traditional use of E. cordatum in South Africa against female infertility has been recorded. Nevertheless, no published study demonstrates this potential till now.

**Antiosteoporosis Activity**

Osteoporosis is a skeletal disorder characterized by a deterioration of bone tissue and disruption of bone microarchitecture that lead to low bone mass and strength, predisposing to an increased risk of fracture (Pisani et al., 2016). It affects both sexes and is mainly linked with the age-related decrease of estradiol and testosterone. Therapeutic agents that would not only inhibit bone resorption but also simultaneously stimulate bone formation would be most favorable (Abdelsamie et al., 2019).

Using a well-known postmenopausal-like model of osteoporosis (ovariectomy) in rats, Ateba et al. (2013) evaluated the effects of a 9-weeks oral treatment with a methanolic extract of the aerial parts of E. laurentii. The extract significantly increased the dry femur weight (at 50 and 200 mg/kg), and calcium levels in serum (at 50 and 200 mg/kg) and femur (at all tested doses) compared with ovariectomized animals. The serum levels of inorganic phosphorus decreased, while the femur levels increased in a dose-dependent manner. Although the dose of 200 mg/kg was not able to completely reverse the ovariectomy-increased alkaline phosphatase (a biomarker for osteoblastic activity and bone remodeling), it decreased it by ~15%. Based on the increased in femur mass, and femur calcium and inorganic phosphorus contents, the authors concluded that bone formation exceeded resorption suggesting the inhibition of bone resorption and activation of bone formation.

There is growing interest in 17β-hydroxysteroid dehydrogenase type 2 (17β-HSD2), an enzyme able to regulate the intracellular concentration of estradiol and testosterone by transforming them into the less potent forms estrone and androsterone (Marchais-Oberwinkler et al., 2011) in tissues where it is expressed, such as bone (Dong et al., 1998; Eyer et al., 1998). Blockade of this enzyme is thought to increase intracellular estradiol and testosterone, which thereby inhibits bone resorption by osteoclasts and stimulates bone formation by osteoblasts (Abdelsamie et al., 2019). In line with this 17β-HSD2 is more and more considered as target for antiosteoporosis treatment. In an in vitro assay using lysates of cells expressing the recombinant human enzyme 17β-HSD2, Vuorinen et al. (2017) tested 36 hit molecules, including 44 and 73 from E. laurentii. These compounds with respective IC50 values of 1.52 and 2.03 µM were among the most active 17β-HSD2 inhibitors tested. However, they selectively inhibited 17β-HSD1 (that catalyzes the reverse reaction) over 17β-HSD2 and therefore cannot be suitable lead structures for a possible therapeutic use (Vuorinen et al., 2017).

**Erectile Dysfunction and Impotence**

Erectile dysfunction (ED) as well as impotence is a multifactorial (psychogenic, neurogenic, vasculogenic, endocrine/metabolic, end organ disease and iatrogenic) health issue common in 20–30% of adult men worldwide (McMahon, 2019; Taylor et al., 2019). It negatively impacts patient’s sexual satisfaction and psychological well-being, leading to a greater prevalence of anxiety and depression. Lifestyle changes in combination with oral phosphodiesterase type 5 inhibitors (PDE5Is: sildenafil, tadalafil, vardenafil and avanafil) are typically first-line treatments of most etiologies of ED (Hatzimouratidis et al., 2016; Krzastek et al., 2019; Moses et al., 2019). PDE5Is increase arterial blood flow into the penis (via relaxation of the corpus cavernosum and deep penile artery smooth muscles) and reduce the venous outflow leading to the penile erection. Among PED5Is, only sildenafil is cost-effective as it is the only PDE5-I with a generic option. PED5Is are commonly associated with side effects (flushing, hypotension, headache, dyspepsia, back pain, myalgia, dizziness, blurred vision and rhinitis) and a lot of contraindications that contribute to significant treatment dropout rates (Yuan et al., 2013; Yafi et al., 2018). Moreover, up to 40% of ED patients fail to respond sufficiently to the maximum dose of PDE5Is (Porst et al., 2013).

From ancient times, plants have served as a dependable source of medicines for treating ED. In the Eriosema genus, E. cordatum, E. kraussianum and E. salignum are traditionally or locally used as aphrodisiac or against male sexual disorders (ED, impotence). However, only compounds from E. kraussianum were evaluated until now. In 2002, Drewes et al. investigated the capacity of
pyrano-isoflavones 64–68 to relax the corpus cavernosum of rabbits. Compounds 64 and 65 displayed a dose-dependent activity, while 66–68 were inactive. At the low concentration of 78 ng/ml, 64 and 65 displayed 85 and 65% of the relaxation found with sildenafil citrate, respectively. Rather to induce relaxation, 66 and 68 caused contraction of corpus cavernosum tissue (Drewes et al., 2004). Accordingly, the authors indicated that the overall effect of the extract as used in traditional medicine is mainly determined by the activities of 64 and 65, present as the major constituents.

Eriosema cordatum, E. kraussianum and E. salignum and the other Eriosema species that come under the isiZulu indigenous umbrella name of “uBangaala” are widely traditionally used mainly in South Africa for curing or alleviating ED and/or impotence (Bryant, 1966; Hutchings et al., 1996). However, despite their high reputation in that domain, the investigation only focused on E. kraussianum with two papers published more than 15 years ago. In line with these, Eriosema species traditionally used against ED remain underexplored and even seem to be abandoned. Given the burden of this sensitive topic, they require more research attention.

Hypoglycemic and Anti-diabetic Effects

Diabetes is a major global health threat. This metabolic disorder is caused by a lack (absolute or relative) of insulin and/or resistance to insulin that lead to chronic hyperglycemia. ED is a common comorbidity of diabetes mellitus. It can be caused by impaired hemodynamic mechanisms in the penile and ischemic vasculature that occur in diabetes mellitus (Rendell et al., 1999). There is a consensus that lifestyle changes and risk factor modification must precede or accompany any pharmaceutical or psychological ED treatment (Hatzimouratidis et al., 2016; Hackett et al., 2018). In other words, the amelioration of diabetes risk factors may improve erectile function. Acute oral treatment with a E. kraussianum rootstock hydro-alcoholic extract (40–320 mg/kg) dose-dependently and significantly reduced fasting blood glucose levels in normoglycemic and streptozotocin-treated diabetic rats from 2 to 8 h after treatment with peak effects after 4 h (Ojewole et al., 2007). Using an oral glucose tolerance test, a pretreatment with the extract 20 min before challenge significantly reduced the peak blood glucose levels. Similar effects were obtained with 80 mg/kg p.o. of kaursiannones 1 and 2 in normoglycemic rats (Ojewole et al., 2006).

In alloxan-induced diabetic Wistar rats, both aqueous and ethanolic leaf extracts of E. psoraleoides (at 200 and 400 mg/kg) significantly decreased fasting blood glucose levels from day 6 of a 7-days treatment (Nduka et al., 2018; Nduka et al., 2019). Using the same model, Elechi et al. (2019) investigated the effects of n-hexane, n-hexane/dichloromethane (1:1 v/v), dichloromethane, and dichloromethane/methanol (19:1 v/v) fractions of the n-hexane leaf extract of E. psoraleoides on the fasting blood glucose levels. The n-hexane/dichloromethane and the dichloromethane fractions at the dose of 200 mg/kg produced a significant decrease in fasting blood glucose levels from day 2–7, the effects of the dichloromethane fraction being higher or very close to that of 4 mg/kg glibenclamide (Elechi et al., 2019).

Eriosema glomeratum claimed to be traditionally used against diabetes (Lawin et al., 2015) is not yet investigated in relation to the metabolic disorder.

Cardiovascular protection: dyslipidemia, vasodilatation and preeclampsia

Cardiovascular disease remains the leading cause of death worldwide (Global Burden of Disease Study 2017; Causes of Death Collaborators, 2018). Managing its modifiable risk factors such as hypertension and dyslipidemia constitutes key targets of public health organizations over the world (Berman et al., 2019; Michos et al., 2019).

Increased risk of cardiovascular diseases such dyslipidemia is well known to be associated with menopause. Using a postmenopause-like model (ovariectomized Wistar rats), a 9-weeks oral treatment with a methanol extract of the aerial parts of E. laurentii significantly decreased the total cholesterol (TC) and LDL levels at 200 mg/kg. Increased HDL as well as a non-significant decrease of triglycerides (TG) levels were also observed at all tested doses (50, 100 and 200 mg/kg). The extract decreased the ovariectomy-increased TC/HDL and LDL/HDL ratios. A significant decrease of the atherogenic plasma index [AIP: log10 (TG/HDL)] was determined at all tested doses (Ateba et al., 2013). Individual cholesterol risk factors are not sufficient to assess cardiovascular risk (Michos et al., 2019). A huge body of evidence supports AIP as one of the strongest predictive indicator of cardiovascular disease risk (Dobiášová et al., 2004; Edwards et al., 2017) also in postmenopausal women (Wu et al., 2018; Barua et al., 2019). This parameter has been evaluated in the study by Ateba et al. (2013) indicating the potential of E. laurentii in the management of dyslipidemia in postmenopausal women.

Ojewole et al. (2006) investigated the vasodilatory effects of 64 and 65 (100–2,000 μg/ml) from the rootstock of E. kraussianum in isolated portal veins. Both constituents, after provoked initial slight contraction, induced a dose-dependent secondary and pronounced vasorelaxant effect, probably by affecting calcium mobilization and/or sequestration, and possibly also, calcium release from its various tissue stores.

Preeclampsia is the most common pregnancy-related complication worldwide, affecting 5–7% of all pregnancies with estimated 70,000 maternal deaths and 500,000 fetal and neonatal deaths each year (Rana et al., 2019). This incidence probably remains underestimated due to underreporting (Mayrink et al., 2018). The options for prevention and treatment of this hypertensive disorder are extremely limited, especially in resource-limited settings (Lemoine and Thadhani, 2019) where almost all of the deaths occur (Oyston and Baker, 2020). In this context, medicinal plants and herbs are an opportunity. In preeclampsia, the abnormal placentation characterized by impaired spiral artery remodeling lead to an ischemic placenta, which releases factors such as anti-angiogenic factors sFlt-1 (soluble fms-like tyrosine kinase-1) and sEng (soluble Endoglin), responsible for vascular dysfunction, into the maternal circulation (Chang et al., 2018; Eddy et al., 2018; Jena et al., 2020). Based on the vasodilatory properties of 65
(Drewes et al., 2002; Ojewole et al., 2006), Ramesar et al. (2012) investigated its effects in the L-NAME-induced preclamptic Sprague-Dawley rat model. Subcutaneously administrated at 10 mg/kg for 12 consecutive days, the compound decreased fetal mortality, demonstrated a trend toward increasing birth and placental weights by improving placental perfusion, reducing blood pressure amplification through a NO-independent mechanism, and decreasing the plasma levels of sFlt-1 and sEng.

Generally, based on the in vivo models used and the results obtained, the investigated Eriosema species display a potential in the management of modifiable risk factors (hypertension, dyslipidemia) of the cardiovascular disease.

**Acetylcholinesterase Inhibition**

The inflammation-associated cognitive decline is mainly due to degeneration of central cholinergic neurons or cholinergic impairment, making acetylcholinesterase inhibitors the main class of drugs currently used in the treatment of mild cognitive impairment and Alzheimer’s disease (Benfante et al., 2019). In a study by Ndhlala et al. (2011), an aqueous extract of the roots of *E. cordatum* with an IC₅₀ value of 756.6 μg/ml showed a very low acetyl cholinesterase inhibitory activity.

**Anti-Microbial Activity**

Infectious diseases are among the most important cause of morbidity and mortality worldwide. This is worsened by drug resistance, one of the greatest challenges of the 21st century (Hofer, 2019; Tacconelli and Peziani, 2019). The importance of plants as a source of effective anti-microbial agents is well established. Several reports dealing with the anti-bacterial and anti-fungal effects of Eriosema species have been documented.

Flavonoids from the roots of *E. chinense* were tested against Gram-negative (Escherichia coli 25,922, Klebsiella pneumoniae and Pseudomonas aeruginosa) and Gram-positive (Bacillus cereus, Enterococcus faecalis, Staphylococcus aureus, methicillin-resistant S. aureus (S. aureus MRSA), Staphylococcus epidermidis, Streptococcus agalactiae, Streptococcus pyogenes and Listeria monocytogenes) bacteria, and Candida albicans using agar dilution technique. Compound 27 displayed a strong activity (minimum inhibitory concentration (MIC) of 2.3 μg/ml) against *S. agalactiae* and *S. pyogenes*. MIC values of 2.3 μg/ml (toward *S. pyogenes*), 4.7 μg/ml (toward *B. cereus* and *S. agalactiae*) and 9.4 μg/ml (toward *L. monocytogenes*, *S. aureus* MRSA, *S. epidermidis*) were observed with compound 23. Compound 40 displayed MIC values of 4.7 μg/ml toward *B. cereus*, *E. faecalis*, *L. monocytogenes*, and all *Streptococcus* and *Staphylococcus* strains. Compound 25 significantly inhibited the growth of *B. cereus* (MIC of 2.3 μg/ml), *S. pyogenes* (MIC of 2.3 μg/ml), *S. aureus* (MIC of 4.7 μg/ml), *S. aureus* MRSA (MIC of 4.7 μg/ml), *S. agalactiae* (MIC of 4.7 μg/ml), and *E. faecalis* (MIC of 9.4 μg/ml) and *L. monocytogenes* (MIC of 9.4 μg/ml). With 20, a MIC value of 9.4 μg/ml was obtained against *B. cereus*, *S. aureus*, *S. aureus* MRSA, *S. agalactiae*, *S. epidermidis* and *S. pyogenes*, and of 18.8 μg/ml toward *E. faecalis* and *L. monocytogenes*. The standard amphotericin B resulted in a MIC of 0.12 μg/ml against *C. albicans*, while chloramphenicol displayed MIC values of 10 μg/ml against *E. coli* 25,922, *K. pneumoniae*, *B. cereus*, *E. faecalis*, *L. monocytogenes*, *S. aureus* and *S. aureus* MRSA, and of 1 μg/ml toward *S. agalactiae*, *S. epidermidis* and *S. pyogenes* (Thongnest et al., 2013).

Dichloromethane and ethanolic root extracts of *E. cordatum* exhibited moderate antibacterial activities against *S. aureus*, *B. subtilis*, *E. coli* and *K. pneumoniae* (Ndhlala et al., 2011). The ethanol extract showed MIC values of 390 μg/ml toward all these microbial species, while that of the dichloromethane extract were 195 μg/ml against *S. aureus* and *B. subtilis*, and 390 μg/ml against *E. coli* and *K. pneumoniae*. Petroleum ether and water root extracts were not active (MIC ≥1.56 mg/ml) against all the tested microbial species. The MIC of the standard neomycin ranged between 0.8 μg/ml and 1.6 μg/ml (Ndhlala et al., 2011).

The ethanolic root extract of *E. chinense* (Prasad et al., 2013c) as well as its hexane, chloroform and ethyl acetate fractions (Prasad et al., 2013b) displayed MIC >195 μg/ml against reference bacterial strains *E. coli* ATCC25922, Shigella flexneri ATCC12022, *P. aeruginosa* ATCC27893, *S. aureus* ATCC25923 and clinical isolates of *Salmonella typhi*, *Shigella dysenteriae*, *Proteus vulgaris*, *K. pneumoniae*, *Shigella boydii*, *B. cereus* and *E. faecalis*. In these studies, IZ values (24.1–30.7 mm) of the standard ciprofloxacin (0.5 mg/ml) were determined, but MIC values were not stated. Compounds 18, 34, 39 and 40 from the roots of *E. chinense* showed MIC values of 12.5 μg/ml against *Mycobacterium tuberculosis* H37Rv, while that of 23, 27 and 38 were 25 μg/ml. Those of the standards isoniazid and streptomycin were 0.023–0.046 and 0.156–0.313 μg/ml, respectively (Sutthivaiyakit et al., 2009).

Using the disk diffusion method, the essential oil from the fresh leaves of *E. englerianum* (1, 2, 5 and 10 μL/ml) was tested against eight different bacteria (*S. aureus*, *E. coli*, *P. aeruginosa*, *B. subtilis*, *K. pneumoniae*, *P. vulgaris*, *C. sporogenes* and *A. calcoaceticus*). Considered as positive result by authors, a diameter of inhibition zone (IZ) ≥7 mm was observed at 5 μL/ml against *A. calcoaceticus*, and at 10 μL/ml against *C. sporogenes* and *A. calcoaceticus* (Mmbengwa et al., 2009). Against opportunistic fungi, a concentration-dependent inhibition of *C. albicans* (24.2–42.6%), *A. niger* (34.7–49.7%) and *A. flavus* (27.5–39.3%) at concentrations of 1–10 μL/ml was seen, while nystatin inhibited them by 84.3, 76.3 and 76.3%, respectively. However, the concentration of nystatin displaying this activity was not indicated (Mmbengwa et al., 2009).

Through the broth dilution method, the essential oil from the roots of *E. chinense* (1, 2, 5 and 10 μL/ml) was tested against eight different bacteria *S. aureus*, *E. coli*, *P. aeruginosa*, *B. subtilis*, *K. pneumoniae*, *P. vulgaris*, *C. sporogenes* and *A. calcoaceticus*. Considered as positive result by authors, a diameter of inhibition zone (IZ) ≥7 mm was observed at 5 μL/ml against *A. calcoaceticus*, and at 10 μL/ml against *C. sporogenes* and *A. calcoaceticus* (Mmbengwa et al., 2009). Against opportunistic fungi, a concentration-dependent inhibition of *C. albicans* (24.2–42.6%), *A. niger* (34.7–49.7%) and *A. flavus* (27.5–39.3%) at concentrations of 1–10 μL/ml was seen, while nystatin inhibited them by 84.3, 76.3 and 76.3%, respectively. However, the concentration of nystatin displaying this activity was not indicated (Mmbengwa et al., 2009).

The standard ciprofloxacin displayed MIC values of 78 and 1.5 ng/ml, respectively. Compounds 1, 2, 13, 47 and 85 from the methanol/ethylmethane (1:1 v/v) extract of the whole plant of *E. glomeratum* were tested at a concentration of 1 μg/ml.
against bacteria (*Bacillus megaterium, E. coli*), the green alga *Chlorella fusca* and the fungus *Microbotryum violaceum* using an agar diffusion assay (Awouafack et al., 2008). Compound 1 displayed IZ of 7 mm toward *B. megaterium, C. fusca* and *M. violaceum*, and of 10 mm against *E. coli*. IZ values of 10, 8, 9 and 13 mm were observed with 2 against *B. megaterium, E. coli, C. fusca* and *M. violaceum*, respectively. Compounds 13 and 47 were only active (IZ of 10 mm) against *C. fusca*, while 85 was inactive against all four microbial species. In this study, the standards were also tested at a concentration of 1 µg/ml. Tetracycline displayed IZ of 18 mm against bacteria, while an IZ of 20 mm was observed with nystatin agains *M. violaceum*. The IZ of the standard actidione was 35 and 50 mm against the alga and fungus, respectively (Awouafack et al., 2008).

A polar fraction of an ethanolic leaf extract of *E. montanum* displayed a low antimicrobial activity with a MIC > 750 µg/ml against bacteria (*B. cereus* ATCC 14579, *Enterobacter cloacae* ATCC 13047, *E. coli* ATCC 8739, *K. pneumoniae* ATCC 13883, *Myco bacterium fortuitum* ATCC 6841, *P. vulgaris* ATCC 13315, *P. aeruginosa* ATCC 15442, *Salmonella typhimurium* ATCC 13311, *S. aureus* ATCC 6538, *Streptococcus pyogenes* ATCC 12344) and fungi (*C. albicans* ATCC 10231, isolates of *Trichophyton rubrum* RV 58125, *Epidermophyton floccosum* RV 71625 and *Microsporum canis* RV 66973) (Cos et al., 2002b).

 METHANOLIC EXTRACTS OF THE BARK AND WOOD OF TWIGS OF *E. psoraleoides* displayed very high MIC values (≥1.25 mg/ml) against *Streptococcus mutans* HG 982, *Actinomyces viscosus* HG485 and *C. albicans* HG392 in the agar dilution method (Khan et al., 2000). MIC values of 8, 32 and 128 µg/ml against these microorganisms were observed with the standard chlorhexidine, respectively. Using a bioautography agar overlay method, Runyoro et al. (2006) reported that a methanolic extract of the stem bark of *E. psoraleoides* was not active against *C. albicans*. A methanolic leaf extract as well as its n-hexane and ethyl acetate fractions were tested against *E. coli* ATCC35219, *S. aureus* ATCC25923 and clinical isolates of *S. aureus, P. vulgaris, Klebsiella aerogenes, P. aeruginosa* and *C. albicans* and displayed MIC >1.26 mg/ml, except the n-hexane fraction with a MIC value of 150 µg/ml toward *S. aureus* ATCC. The MIC value of the standard gentamicin was not reported (Elechi and Igboh, 2017).

An anetholic extract from the twigs of *E. robustum* showed a MIC value of 80 µg/ml against *S. aureus, E. faecalis* and *E. coli* and of 310 µg/ml toward *A. pyrogensosa*. Significant differences in the activity were observed against the fungi *Aspergillus fumigatus* (MIC 160 µg/ml), *Cryptococcus neoformans* (MIC 630 µg/ml), *C. albicans* and *C. albicans* ATCC (MIC 1,250 µg/ml) (Awouafack et al., 2013a). Compounds from this extract showed either moderate or low activity against these microbial species. Moderate antimicrobial activities (MIC 63 or 65 µg/ml) were observed with 16 and 17 against *C. albicans* ATCC, *A. fumigatus* and *P. aeruginosa*. 17 also showed a moderate activity against *Cryptococcus neoformans* and *E. faecalis*. A MIC of 63 or 65 µg/ml was observed with 107 against *P. aeruginosa* and with 87 against *A. fumigatus* and *P. aeruginosa*; 101 against *C. albicans* ATCC and *P. eruginosa*; 99 against *S. aureus* and *P. aeruginosa*; 88 against *A. fumigatus*, *C. neoformans*, *P. aeruginosa* and *E. faecalis*; 41 against *C. albicans* ATCC, *S. aureus*, *P. aeruginosa*, *E. faecalis* and *E. coli* (Awouafack et al., 2013a). The standard gentamicin showed a MIC < 3.91 µg/ml against bacteria, while that of amphotericin B was 30 µg/ml toward *C. albicans* (isolate) and *C. albicans* (ATCC), >250 µg/ml against *C. neoformans* and 125 µg/ml against *A. fumigatus*. Using a microdilution method, 5 and 72 from the ethanol extract of twigs of *E. robustum* displayed weak antimicrobial activity (MICs >150 µg/ml) against *Bacillus subtilis, S. aureus, K. pneumoniae, E. coli, C. albicans*, and *Saccharomyces cerevisiae* (Awouafack et al., 2018) In this study, the tested concentrations or MIC values of standard antibiotics ampicillin, kanamycin, and cycloheximide were not indicated.

Using the broth microdilution method, the antifungal activity of methanolic leaf extracts (500 µg/ml) of *Eriosema campestre* var. *campestre, Eriosema campestre* var. *macrophyllum, Eriosema glabrum* Mart. ex Benth., *Eriosema heterophyllum* Benth., *Eriosema longifolium* Benth. and *Eriosema tacuaremboense* Arechav. was evaluated. After 72 h incubation, *E. heterophyllum* was fungistatic against *T. rubrum*, *Trichophyton mentagrophytes* and *Microsporum gypseum* and fungicidal against *Epidermophyton floccosum*. The extracts of *E. campestre* var. *macrophyllum* and *E. glabrum*, respectively, displayed fungistatic and fungicidal activities against *T. mentagrophytes* and *E. floccosum*. The extract of *E. campestre* var. *campestre* was fungistatic toward *T. rubrum*, *T. mentagrophytes* and *E. floccosum*. Moreover, all these *Eriosema* species were not active against *C. albicans, Candida krusei, Candida glabrata, Candida tropicalis* and *Candida parapsilosis* after 48 h incubation (de Morais et al., 2017).

The bioassay-guided fractionation of a dichloromethane root extract of *E. tuberosum* using a TLC bioautography assay led to the isolation of compounds 34–36, 40, 62 and 75. Amounts of 5 µg of 35, 36, 40 and 62, and 10 µg of 34 on TLC plates prevented the growth of *Cladosporium cucumerinum*, while 1 µg of 34, 36, 40 and 62, and 5 µg of 35 inhibited the growth of *Candida albicans*. *Eriosematin* (75) was not active against *C. cucumerinum* and *C. albicans* (Ma et al., 1995). 77 from the same extract inhibited the growth of both fungi at 2.5 µg, while 76, 78 and 79 were not active (Ma et al., 1996a). Compounds 80 and 81 exhibited a strong activity (inhibition at 0.5 µg) against *C. cucumerinum* and a weak activity (inhibition at 30 µg) against *C. albicans* (Ma et al., 1996b). Moreover, 10 and 30 µg of 39 were active against *C. cucumerinum* and *C. albicans*, respectively. In the same assay, 2 µg of 98 and 3µg, each, of 94, 96 and 104 inhibited the growth of *C. cucumerinum*, 82, 105 and 106 were not active against *C. cucumerinum* (Ma et al., 1999).

A study by Sianglum et al. (2019), lupinifolin (39) demonstrated an antimicrobial activity against *E. faecalis* ATCC29212, *S. aureus* ATCC25923 as well as susceptible and multidrug-resistant enterococcal clinical isolates (*E. faecalis* and *E. faecium*) in the standard broth microdilution method. Although the tested compound was not extracted from an *Eriosema* species, it has been reported in roots of *E. chinense* and *E. robustum*. In that study, 39 displayed activity against all susceptible and resistant strains with MICs and MBCs (minimum bactericidal concentration) ranging between 0.5 and 2 µg/ml and between 2 and 16 µg/ml, respectively. Toward all the strains, compound 39 with MIC values of 0.5–2 µg/ml was more active
than vancomycin (MIC of 1–256 μg/ml). It increased membrane permeability and caused loss of salt tolerance. On *E. faecalis* ATCC29212, *E. faecalis HTY0037* (a multidrug resistance isolate) and *E. faecium* HTY0256 (a strong biofilm-producing vancomycin-resistant enterococci isolate), after 2 h incubation it displayed significant rapid antibacterial activity. Moreover, an antibiofilm-producing activity of 39 against four enterococci was shown.

Eighteen articles dealing with the antimicrobial activity of *Eriosema* species have been published using disk diffusion, broth dilution and thin layer chromatography (TLC) bioautography methods. The “traditional” inhibitory zone (IZ) determined by the disc diffusion method depends on the coefficient of diffusion of compounds, highly polar substances diffusing more easily in agar and displaying a high IZ and vice versa (Tan and Lim, 2015). Therefore, this assay is only useful for a simple qualitative screening as it does not allow the determination of the real amount of the antimicrobial agent that diffuses into the agar, impeding the determination of MICs and MBCs (Balouiri et al., 2016). Based on the MIC values, extracts (or compounds) display: i) a strong antimicrobial activity in vitro if the MIC ≤100 μg/ml (or 10 μg/ml), ii) moderate if 100 < MIC ≤625 μg/ml (or 10 < MIC ≤100 μg/ml), iii) and low if MIC > 625 μg/ml (or >100 μg/ml) (Eloff, 2004; Ríos and Recio, 2005; Kuete, 2010). Based on this classification, several extracts and compounds from *Eriosema* species displayed promising antimicrobial activity. Unfortunately, in several studies positive controls were not included or their concentration was not stated. Although some studies are suggesting the potential of few compounds to act as an antimicrobial drug against several microorganisms, these deficiencies weaken the evidence.

**Anti-Viral Activity**

Cos et al. (2002a) assessed the anti-human immunodeficiency virus type-1 (HIV-1) effects of a polar fraction of an ethanolic leaf extract of *Eriosema montanum* Baker f. using a tetrazolium-based colorimetric assay in infected MT-4 cells. The polar fraction was obtained suspending the extract in 60% methanol and defatting with petroleum ether. The polar fraction with an EC50 value >166 μg/ml did not protect the HIV-infected cells.

At the maximal non-toxic concentrations of 375 μg/ml, this polar fraction exhibited a pronounced antiviral activity (reduction factor of the viral titer (RF) of 10^3 – 10^4) against Herpes simplex virus type 1, Poliomyelitis virus type 1 strain 1A/S3 and Semliki forest virus A7, while at 187.5 μg/ml it displayed a RF of 10^3 against Coxsackie B2 virus. RF values of 10^2 were observed against Vescicular stomatitis virus T2 and measles Edmonston A at 187.5 and 750 μg/ml, respectively (Cos et al., 2002b).

**Anti-Diarrheal Activity**

Diarrheal diseases are a leading cause of mortality and morbidity worldwide, mainly among children under-five in low developing countries. Defined as the discharge of 4 or more semisolid or watery feces per day, diarrhea involves an increase in intestinal fluid volume, in the frequency of bowel movement, wet stool and abdominal cramps, leading to loss of electrolytes and water. Its treatment and management depend on the duration and specific etiology which can be infectious or not. Over the world, many people or communities still use traditional herbs to treat a variety of diseases including diarrhea. As depicted in Table 1, several *Eriosema* species are used traditionally for diarrhea.

Castor oil-induced diarrhea is known as an efficient model for the initial screening for antimitotility, antisecretory and anti-inflammatory compounds. In the gut, ricinoleic acid (castor oil metabolite) causes irritation and inflammation in bowels leading to diarrhea (stomach cramp, increased peristaltic activity and intestinal fluid volume) (Matias et al., 1978; Racusen and Binder, 1979). An ethanol root extract of *E. chinense* (EEC; at 400 mg/kg), its chloroform fraction (at 100 mg/kg; CEC), and compounds 39 and 81 (at 10 mg/kg) reduced the normal fecal excretion rate and water content 3, 5 and 7 h after the oral treatment of rats. In castor oil-induced diarrhea, these treatments delayed the onset of diarrhea and decreased the mean defeation in a dose-dependent manner. At the same dosages, the extract, the fraction and 39 and 81 significantly reduced the peristaltic index, the intestinal fluid volume and PGE2-induced enteropooling, and demonstrated a significant recovery from intestinal fluid loss of Na^+ and K^+ (Prasad et al., 2013c; Prasad et al., 2017).

Enteropathogenic *E. coli* (EPEC) is a common cause of moderate to severe water diarrhea in children, accompanied with fever, vomiting and a high hazard of death. In an enteropathogenic *E. coli*-induced diarrhea rat model, EEC (100 and 200 mg/kg), CEC (50 and 100 mg/kg) and 81 (5 and 10 mg/kg) induced a significant recovery from diarrhea characterized by the reduction in total number of stools, total number of diarrheal stools, weight of stools, mean defeation rate and water content of stools 6 h after induction of diarrhea (Parmar et al., 2019a; Farmar et al., 2019b). At the higher tested doses, EEC, CEC and eriosematin E displayed diarrhea scores very close to that of 5.7 mg/kg norfloxacin. They also increased Na^+ /K^+-ATPase activity to a higher level than that observed in the normal rats, resulting in reduced intestinal secretion.

Both infectious and non-infectious (chemically induced) reliable models were used to evaluate the anti-diarrheal potential of *Eriosema* species in vivo. However, from five species traditionally claimed to be anti-diarrheal (*E. affine*, *E. chinense*, *E. griseum*, *E. psoraleoides* and *E. tuberosum*), only the ethanolic root extract of *E. chinense* and compounds 39 and 81 were investigated, indicating that in the *Eriosema* genus this domain is underexplored. Given the promising results obtained with one extract, it would be interesting to extend the exploration to the other *Eriosema* species traditionally used against diarrhea.

**Anti-Inflammatory Activity**

Intestinal disorders often co-occur with inflammation and dysmotility. In enteropathogenic *E. coli*-induced diarrhea, 10 mg/kg of 81 from roots of *E. chinense* for 24 h significantly decreased the expression of pro-inflammatory cytokines IL-1β and TNF-α in colonic tissues (Parmar et al., 2019b).
Using peripheral blood mononuclear cells, Santos et al. (2016) investigated the impact of a dichloromethane-ethanol extract of *E. campestre* (6.25, 12.5 and 25 μg/ml) on pathological processes of chronic inflammatory diseases. In a concentration-dependent manner, the extract inhibited the proliferation of T lymphocytes, including CD4+ and CD8+ cells, and decreased IL-2 levels in the supernatant of the cell cultures, a cytokine essential for the expansion of T lymphocytes.

Cyclooxygenase (COX) inhibitors are known to be a therapeutic target in inflammatory and neuroinflammatory diseases (Grosser et al., 2017; Dhir, 2019). The COX-1 and COX-2 inhibitory activities of extracts of the roots of *E. cordatum* were investigated by Ndhlala et al. (2011). At 250 μg/ml, petroleum ether, dichloromethane and ethanolic extracts weakly inhibited COX-1 activity by 13, 25 and 34%, respectively. A weak inhibition of COX-2 by 6, 35 and 10%, respectively, with 250 μg/ml of the petroleum ether, dichloromethane and ethanolic extracts was observed. The aqueous extract remained almost without effects on both enzymes at 2 mg/ml.

**Anthelmintic Activity**

Among human helminth infections, schistosomiasis is the most prevalent with regard to mortality and the third most harmful tropical disease in the world. An ethanol leaf extract of *E. griseum* was tested in vitro against trematodes (*Echinostoma caproni* and *Schistosoma mansoni*) and nematodes (*Ancylostoma ceylanicum*, *Heligmosomoides bakeri* and *Trichuris muris*). The extract reduced the motility of third-stage larvae (L3) of *H. bakeri* by at least 80% at a minimal lethal concentration (MLC) of 20 μg/ml 48 h post-incubation, caused death of newly transformed *S. mansoni* schistosomula and adults with MLC values of 20 and 40 μg/ml, respectively, exhibited a moderate activity against L3 of *A. ceylanicum* 48 h post-incubation and no activity on adult *E. caproni* and *T. muris* (MLC: 2 mg/ml). *In vivo*, mice harboring adult *S. mansoni*, *E. caproni* and *T. muris* were used. An oral single dose of the extract (400 mg/kg) 49 days post-infection displayed a moderate activity in chronic *S. mansoni* infection (reduction of total worm burden 49.5% and of female worm burden 48.9%), whereas no activity was observed against *E. caproni* and *T. muris* at 400 and 800 mg/kg, respectively (Koné et al., 2012).

**TOXICOLOGICAL EVALUATION**

Although medicinal plants are widely used and assumed to be safe, however, they can potentially be toxic (Nasri and Shirzad, 2013; Awounfack et al., 2016). “If herbs have an effect, they are also likely to have a side effect” (Lanini et al., 2012). In line with this, the safety evaluation of medicinal plants—even used since centuries—needs to be performed. *In vitro* and *in vivo* studies have been carried out aiming at the evaluation of the safety properties of some *Eriosema* species.

In the Ames test on *Salmonella typhimurium* strain TA98 with and without S9 metabolic activation, a water extract of the roots of *E. cordatum* at concentrations up to 5,000 μg/ml was non-mutagenic as shown by the average His+ revertant colonies (Ndhlala et al., 2011).

According to Koné et al. (2012), an ethanolic leaf extract of *E. griseum* displayed no toxicity against L6 rat skeletal myoblast cells. Awouafack et al. (2013a), evaluated the cytotoxicity of an ethanolic twig extract of *E. robustum* and compounds thereof against normal monkey Vero cells. In the MTT assay, the extract showed a low cytotoxicity (IC50 of 53.45 μg/ml). Among isolates obtained from this extract, 88 and 107 were not cytotoxic, 17, 41, 87 and 101 displayed a low cytotoxicity (21.87 ≤ IC50 ≤ 91.52 μg/ml), while 16 was moderately cytotoxic (IC50 of 13.20 μg/ml).

*In vivo*, the acute oral toxicity of an ethanol root extract (EEC) of *E. chinense* and its chloroform fraction (CEC) was evaluated in female rats following the OECD (Organization for Economic Cooperation and Development) guideline 425. Administration of
EEC and its subfractions did not cause any signs of toxicity or mortality up to 2 g/kg during the observation period of 14 days (Prasad et al., 2013b).

In a study by Ateba et al. (2014a), the toxicity of a methanol extract of the aerial parts of *E. laurentii* following guidelines for acute (OECD guideline 423) and subchronic (OECD guideline 407) oral administrations was investigated. A single dose of 2 g/kg of the extract as well as the repetition of the experiment, caused neither toxicological symptoms nor mortality and the LD50 was estimated >5 g/kg. In 28-days repeated oral administration, no signs of toxicity were observed phenotypically and in the main organs of rats. The extract only induced a delayed decrease of relative spleen weight and reduced the white blood cell count in males at the highest dose of 400 mg/kg.

Using the Irwin test, Prasad et al. (2017) showed that the acute oral administration of 81 (from the roots of *E. chinense*) up to 300 mg/kg did not result in any sign of behavioral/neurological toxicity or mortality during the observation period. The weight of organs was not affected. Some signs of physical toxicity were observed at the dose of 500 mg/kg.

Nduka et al. (2018) reported LD50 values of 3807.9 mg/kg and >5,000 mg/kg for ethanolic and aqueous leaf extracts of *E. psoraleoides*, respectively, following an acute oral treatment.

Toxicological evaluations are of major importance for medicinal plants and herbal products. Without these studies the estimation of their therapeutic potential is limited when the doses to induce non-fatal as well as fatal adverse effects are unknown. Based on the *in vivo* acute toxicity studies, the tested extracts of *E. chinense*, *E. laurentii* and *E. psoraleoides* are placed at category 5 (or unclassified) in the Globally Harmonized Classification System for Chemical Substances and Mixtures (GHS) as adopted by OECD (OECD, 2001). Such products with no deaths up to 2000 mg/kg (estimated LD50 > 5000 mg/kg) are considered practically non-toxic (Hodge and Sterner, 1949; Kennedy et al., 1986).

**CONCLUSION**

In this paper, we reviewed the available information concerning the traditional uses/ethnopharmacology, phytochemistry, pharmacology and toxicology of the genus *Eriosema*. Twenty-five species (~16.6% of the genus) recorded in the review are known as traditional medicines and used for nearly 121 ailments. It is evident from anecdotical notes that the investigated numbers of species and traditionally treated health problems are so far lower than the reality. Moreover, around 75% of the traditional indications of these plants have not been studied yet in respective pre-clinical studies, indicating that more scientific investigations are necessary. Apart from data on ethnopharmacology, only 49 papers dealing with the phytochemical, pharmacological and toxicological investigation and reviews on *Eriosema* species and compounds occurring in this genus have been published in 25 years (Figure 4). The mean rate of approximately 2 publications per year is very low. Despite the high reputation of several species for curing or alleviating ED/impotence, especially in Africa, the investigation is only limited to two papers on *E. kraussianum* which have been published more than 15 years ago indicating an unexplored aspect that requires more research attention. Concerning phytochemistry, the paper covers a total of 107 compounds mainly belonging to the classes of flavonoids, chromones and terpenoids. The pharmacological activities of extracts and pure compounds from this genus focused on the management of erectile dysfunction, pre-eclamptic complications and anti-diabetic, estrogenic, hypolipidemic, anti-oxidant, anti-microbial, anti-osteoporosis, anthelmintic, anti-diarrheal and anti-cancer effects as well as cyclooxygenase and acetylcholinesterase inhibitory properties. However, there is lack of studies dealing with the in-depth mechanisms involved in the observed activities *in vitro* and in animals. Moreover, no clinical study has been carried out till now. Beyond the pharmacological activities, the toxicity evaluation of medicinal plants is of high importance for their valorization. *In vivo*, acute toxicity carried out with *E. chinense*, *E. laurentii* and *E. psoraleoides* indicated a low toxicity of investigated extracts.

**AUTHOR CONTRIBUTIONS**

SA obtained literatures, wrote the first draft, and edited the manuscript; DN gave ideas and critically reviewed the manuscript; LK obtained the literatures, gave ideas, critically reviewed and edited the manuscript. All authors read and approved the manuscript.

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Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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