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PHARMACOLOGICAL AND CHEMOTAXONOMIC ASPECT OF TERPENES IN *SECURINEGA VIROSA*

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ABSTRACT

Securinega virosa is synonymous to *Flueggea virosa*, it could be used interchangeably. Many studies have shown that *Securinega virosa* is a natural source for alkaloids, these alkaloids are term Securinega alkaloids. Though, many other compounds have been isolated from this medicinal plant i.e. flavonoids, phenolics and terpenes. Alkaloids have been established as a chemotaxonomy marker for this species since this medicinal plant is a component in most herbal products. This review seeks to establish the friendly connection between this plant and terpenoids by explicitly stating the pharmacological importance of this class of compounds in this species, which suggest the nature and property of terpenoids and also giving an update on the isolated terpenoids (about fourty-one (41) isolated so far). Also to clarify that beside alkaloids compounds, terpenoids could be used also as a chemotaxomic marker for this plant.

Keywords: *Securinega virosa; Flueggea virosa; alkaloids; terpenoids; polyphenols*

INTRODUCTION

From species *Flueggea*, *Phyllanthus* and *Securinega*, many alkaloids have been isolated termed Securinega alkaloids. This class of secondary metabolites is fascinating group of compounds mostly from Euphorbiaceae family (Beutler and Brubaker, 1987; Snieckus, 1973). Some authors first isolated securinine, an example of these compounds for over sixty years ago, from *Securinega suffructiccosa* in 1956 (Murev'eva and Ban'kovskii, 1956). Alkaloids of these type includes pyrrolizidine (norsecurinine-type) heterocycle/ an (securinine-type) indolizidine and α, β, γ, δ-conjugated lactone fragment to form a highly rigid tetracyclic skeleton (Zhang *et al.,* 2013). Securinega alkaloids have received wide and interesting attention from scientists in the field of drug discovery because of their intriguing features and significant pharmacological properties. Many authors have established that these compounds possess activities such as anti-HIV, antitumour and anticancer, antiarrhythmic and anti-hepatitis C virus (Zhang *et al.,* 2015; Zhang *et al.,* 2013; Wehlauch *et al.,* 2016; Tatematsu *et al,* 2006; Monkodkaew *et al.,* 2009; Iketuboisin and Mathieson, 1963). These alkaloids have been known to this genus for a very long time hence they also serve as a chemotaxonomic marker for the species in the genus. Siddiqui *et al.* (2017) reported two compounds that could serve as biomarker/taxonomic marker for *Securinega virosa* because this plant species is in use by in many herbal products around the world. These compounds are ent-phyllanthidine (**40**) and rutin (**41**), these were isolated from the methanol extract of aerial parts of *Flueggea virosa (*Siddiqui *et al.,* 2017*).* One of the compound is an alkaloid while the other is a flavonoid hence the need to establish the connection between *S. virosa* and terpenoids. Literatures are obvious with the isolation of terpenoids but none seek to emphasize its connection with *S. virosa* hence this study seeks to prove the importance of terpenoids to this genus and exact its uniqueness since about forty-one of this-type of compounds were isolated from them.

REVIEW METHODOLOGY

Relevant literature was collected by searching the major scientific databases including EBSCO, google and google-scholar, Pubmed, PROTA, Medline, SciFinder, Science-direct and SCOPUS, also other Botanical/ plants databases. Many Publications' sites were queried like Springer, Elsevier, and dissertations search engines like Open-thesis, OATD, ProQuest and EthOs were put to use. Various keywords were used: *Securinega virosa*, uses of *Securinega virosa*, biological activity of *Securinega virosa*, terpenoids of *Securinega virosa*.

Ethnobotany and Ethnomedicinal Uses

*Securinega virosa (*Roxb. ex Willd.) Baillon belongs to Euphorbiaceae family and plant order Geraniales. *S. virosa* is the name to the same plant as *Fluggea microcarpa* Blume and *Fluggea virosa* (Roxb. ex Willd.) Baillon. These names could be used interchangeably, many plant search engines confirm this (The Plant List (2013); plants.jstor.org, 2015) *Securinega virosa* (Roxb. ex.Willd.) Baill (Euphorbiaceae) is a flowering shrub that flourishes in the sub-Sahara Africa, it grows up to about 6 m in this region. Many authors have reported its traditional uses in many developing countries. It is employed in Tanzania against chest pain, diarrhoea, dysmenorrhea, edema, epilepsy, gonorrhea, gastrointestinal conditions, renal complaint and rheumatism (Haerdi, 1964; Khan *et al.,* 1978; Sawhney *et al.,* 1978; Hedberg *et al.,* 1983a). Malaria, sexual prowess liver disease, inflammation and pain, removal of worms in the human

body, against bilharziasis, are some of the diseases reportedly manage by *S. virosa* by the locals. It is also used for the treatment of malaria (Hedberg *et al.,* 1983a; Vasileva, 1969; Holdsworth, 1975; Yang *et al.,* 1987; Hedberg *et al.,* 1983b; Berhault, 1971; Hedberg *et al.,* 1983b; Samuelsson *et al.,* 1992). In developing countries i.e. Ghana, Senegal, Tanzania and Zimbabwe, many authors give a report of various part of this medicinal plant traditionally use. Decoction from its roots are employed as aphrodisiac, it leaves and roots are used to against pain in children, help to sleep, the fruits and the stems is used against snake-bite (Dalzel, 1936; Moshi *et al.,* 2000; Neuwinger, 1996; Watt and Breyer-Brandwijk, 1962). Traditional healers in some parts of Nigeria, use its leaves decoction against cancer, roots and twigs concoction is employed against epilepsy and mental illness (Magaji *et al.,* 2008; Soladoye *et al.,* 2010; Yerima *et al.,* 2009).

*Securinega virosa a*nd Vernacular names

This medicinal plant has a string of names by which it is called around the world as illustrated in Table 1. *S. virosa* is commonly referred to as Snowberry tree, white berry bush, Chinese water-berry, simple-leaf bush-weed, common bush-weed in English language.

Table 1: Other names of *Rumexacetosa*

Country	Name	Language	References
Nigeria	*shim shim/camal, cambe, came*	Kanuri/Fulani	Neuwinger, 1996
Nigeria	*tsuwaawun karee, gussu, gwiiwar karee*	Hausa	Neuwinger, 1996
Nigeria	*iranje*	Yoruba	Neuwinger, 1996
Nigeria	*njisinta*	Ibo	Neuwinger, 1996
Vietnam	*bong nô'.*	Vietnamese	Magaji *et al.,* 2014
Indonesia	*simpeureum*	Sundanese	Hedberg *et al.,* 1983b
Indonesia	*sigarjalak, trembilutan*	Javanese	Berhault, 1971
Philippines	*arusit*	Ilokano	Hedberg *et al.,* 1983b
Philippines	*botolan*	Tagalog	http://plants.jstor.org/
Philippines	*tulita-ngalong*	Bisaya	http://plants.jstor.org/
Thailand	*kaangkhaao/ma taek*	General/Northern	http://plants.jstor.org/
Thailand	*daengnam*	Lampang	http://plants.jstor.org/
Ghana	*nkanaa*	*Akan-Asante*	http://plants.jstor.org/
Ghana	*susuwulugu*	*Dagbani*	http://plants.jstor.org/
Ivory coast	*niassulébaka /genakwo*	*Baule/Kru-Bete*	http://plants.jstor.org/
Ivory coast	*Sokulénié/buregnemïé*	*Kulango/Kweni*	http://plants.jstor.org/
Senegal	*l'emleise/bi osì*	*Arabic/Balanta*	http://plants.jstor.org/
Senegal	*Sauda /savda (JB) a-nambarisitèn*	*Banyun/Basari*	http://plants.jstor.org/
Niger	*kartiékartié (Aub.)*	Arabic	http://plants.jstor.org/
Ganbia	*brumbarongo*	*Manding-Mandinka*	http://plants.jstor.org/
Mali	*sɛgɛlɛ (CG) segere*	*Dogon*	http://plants.jstor.org/

Phytochemistry

Chao *et al.,* 2016 isolated these terpenoids: 3α,10α-Dihydroxy-12-methoxy-13-methyl-9(10/20)-abeoent- podocarpa-8,11,13-triene (**1**), 3β,10α,12-Trihydroxy-13-methyl-9(10 / 20)-abeo-entpodocarpa- 6,8,11,13-tetraene (**2**), 3β,10α-Dihydroxy-12-methoxy-13-methyl-9(10 / 20)- abeo-ent-podocarpa-8,11,13-triene (**3**), 10α-Hydroxy-12-methoxy-13-methyl-9(10 / 20)-abeo-entpodocarpa-6,8,11,13-tetraen-3-one (**4**), 10α-Hydroxy-12-methoxy-13-methyl-9(10 / 20)-abeo-entpodocarpa-8,11,13-trien-3- one (**5**), 10α,12-Dihydroxy-13-methyl-9(10 / 20)-abeo-

entpodocarpa-6,8,11,13-tetraen-3-one (**6**), 3α,20-Dihydroxy-12-methoxy-13-methyl-ent-podocarpa-6,8,11,13-tetraene (**7**), 3β-Hydroxy-12-methoxy-13-methyl-ent-podocarpa-8,11,13-triene (**8**), 3β-Hydroxy-12-methoxy-13-methyl-ent-podocarpa-6,8,11,13-tetraene (**9**),3α,12-Dimethoxy-13-methyl-ent-podocarpa-6,8,11,13- methyl-ent-podocarpa- 6,8,11,13-tetraene (**9**),3α,12-Dimethoxy-13-methyl-ent-podocarpa-6,8,11,13-tetraene (**10**), 3a,20-Epoxy-3b,12-dihydoxy-13-methyl-ent-podocarpa-8,11,13-triene (**11**), 3α,20-Epoxy-3β,12-dihydroxy-13-methyl-ent-cleistantha-8,11,13,15-tetraene (**12**),12-Methoxy-13-methyl-ent-podocarpa-6,8,11,13-tetraeno-20,3α-lactone (**13**), 12-Hydroxy-13-methyl-ent-podocarpa-6,8,11,13-tetraeno-20,3α-lactone (**14**), 12-Hydroxy-13-methyl-ent-podocarpa-8,11,13-trieno-20,3α-lactone (**15**), 6β-Hydroxy-12-methoxy-13-methyl-ent-podocarpa-8,11,13- trien-3,7-dione (**16**), 6,12-Dihydroxy-13-methyl-7-oxo-ent-podocarpa-5,8,11,13-tetraeno-20, 3α-lactone (**17**), (2R,4S) 2,4-epoxy-4,23,29-trihydroxy- 3, 4-seco-30-norfriedel-19-en-3-oic acid methyl ester (**18**), *p*-bromobenzoate esters(2R,4S) 2, 4-epoxy- 4, 23, 29-trihydroxy-3,4-seco-30-norfriedel-19-en-3-oic acid methyl ester (**19**),*p*-bromobenzoate ester- 6,12-Dihydroxy-13-methyl-7-oxo-ent-podocarpa- 5, 8, 11, 13-tetraeno-20,3a-lactone (**20**) (Chao *et al.,* 2016). Chao *et al.,* 2014 isolated these terpenoids from the roots of *flueggea virosa*, 3β,12-Dihydroxy-13-methylpodocarpa-6,8,11,13-tetraene (**21**), 3β,12-Dihydroxy-13-methylpodocarpa-8,11,13-triene (**22),** Spruceanol (**23**), ent-3β,12α-Dihydroxypimara-8 (14),15-diene (**24**), 3α-Hydroxy-12-methoxy-13-methyl-ent-podocarp- 6,8,11,13-tetraene (**25**), 3α-Hydroxy-13-hydroxymethyl-12-methoxy-ent-podocarp-6,8,11,13-tetraene (**26**), 3β-Hydroxy-13-hydroxymethyl-12-methoxy-ent-podocarp-6,8,11,13-tetraene (**27**), 12-Hydroxy-13-methyl-ent-podocarp-6,8,11,13-tetraen-3- one (**28**), 12-Methoxy-13-methyl-ent-podocarp-6,8,11,13-tetraen-3- one (**29**), 6β,12-Dihydroxy-13-methyl-ent-podocarp-8,11,13-trien-3-one (**30**), 7α, 20-Epoxy-3α-hydroxy-12-methoxy-13-methyl-ent-podocarp- 8,11,13-triene (**31**), 3α,20-Epoxy-3β-hydroxy-12-methoxy-13-methyl-ent-podocarp- 8,11,13-triene (**32**) (Chao *et al.,* 2014). Monkodkaew *et al.,* 2009 isolated five triterpenes from *F. virosa* namely Friedelin **(33**), epifriedelanol (**34**), heptanolide (**35**), betulinic acid (**36**) and stigmasterol (**37**). Magaji *et al.,* 2015 and Pu *et al.,* 2001 isolated a terpenoid from the twigs and leaves of *S. virosa* called Bergenin (**38**) (Fig. **1**)

Pharmacological Importance of Terpenoids Isolated from *S. virosa*

Anti-hepatitis C Virus Activity

Chao *et al.* (2016) reported the anti-hepatitis C virus (HCV) infection to human hepatoma Huh7.5 cells activity of some of the isolated terpenoids. Compounds **8** and **9** displayed a very significant activity toward the virus (Chao *et al.,* 2016).

Antiarrhythmic and Sleep Promoting Effect

Magaji *et al.* (2015) isolated bergenin (**38**) from the root bark of *S. virosa* and evaluated for its sleeping potential. The authors concluded that this compound (**38**) may be responsible for the sedative effect of this medicinal plant. Pu *et al.,* 2001 isolated bergenin (**38**) from the aerial part of *flueggea virosa,* the compound was evaluated against animal dosed cardiac arrhythmic. Bergenin (**38**) prove to be effective as an antiarrhythmic agent (Magaji *et al*. 2015; Pu *et al.,* 2001).

Antiproliferative Activity

Monkodkaew *et al.,* 2009 reported the antiproliferative activity of the five triterpenes that were isolated from *S. virosa.* Their result showed that betulinic acid (**36**) displayed good cytotoxicity activity against the human cancer cell lines used.

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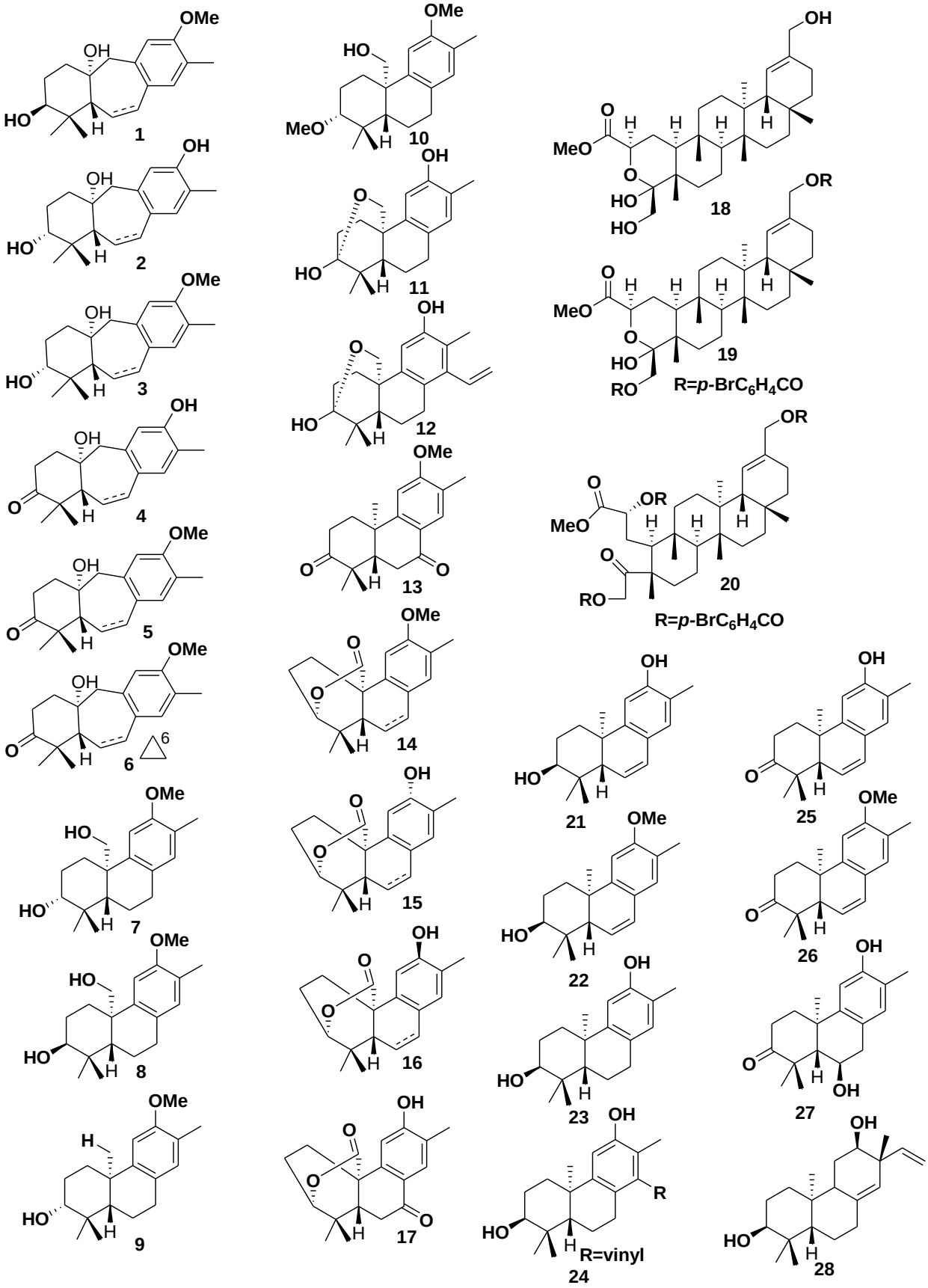
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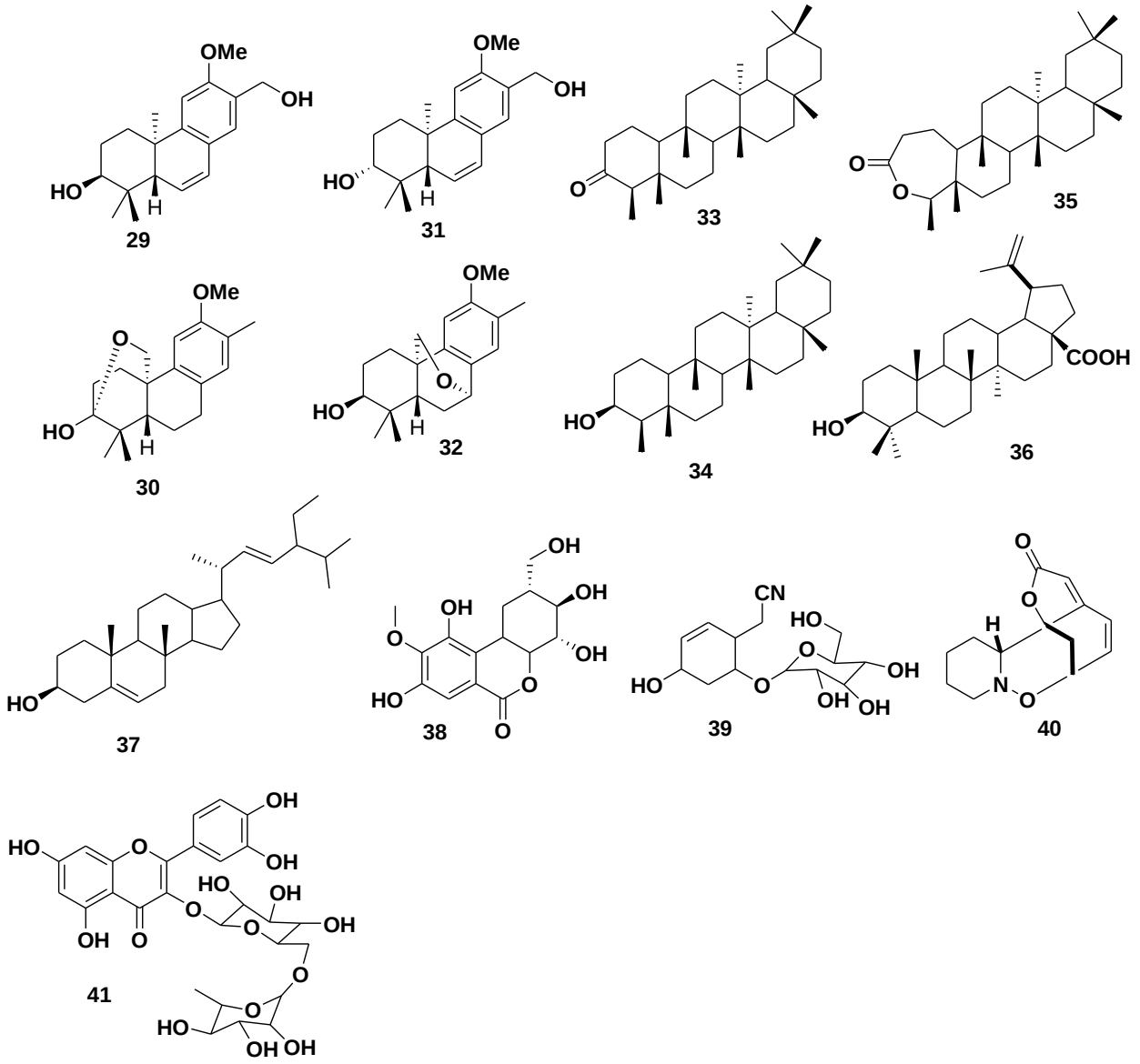

Fig. 1: Isolated Terpeniods from S. virosa

Antiproliferative Activity

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Chemotaxonomic significance

Flueggeae virosa also known as *Securinega virosa* contain terpenoids metabolites, especially different types of diterpenoids. Many authors have isolated these compounds-type from this species, compounds **1 – 20** (Chao *et al.,* 2016), compounds **21 - 32** (Chao *et al*., 2014), compounds **33 -37 (**Monkodkaew *et al.*, 2009), compound **38** (Siddiqui *et al.*, 2015). One or more of these compounds could serve as chemotaxonomy marker for this plant species, bergenin (**38)** or any of the diterpenoids can serve this purpose. Siddiqui *et al.*, (2015) proposed that bergenin (**38**) and menisdaurin (**39**), the latter be a phenolic, Siddiqui *et al.*, 2017 as reported earlier in this study proposed that ent-phyllanthidine (**40**) and rutin (**41**). Hence, terpenoids also could serve as a chemotaxonomic marker for *S. virosa*

CONCLUSION

This review gives the overview of isolated terpenoids from *S. virosa*. About thirty-eight of these compounds have been isolated so far from this medicinal plant. Its use in many and major herbal product calls easy identification based on chemotaxonomy hence this study. Terpenes might aid with growth and impact the plant's reproduction via multifaceted sets of interactions but they may not be significant in determining plants' survival. The result is in relation with the proposed

theory that alkaloids and terpenoids could be of taxonomy importance in this species.

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CONFLICTS OF INTEREST STATEMENT

No potential conflict of interest was reported by the authors.

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