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Natural products potential of the genus Aptenia

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Abstract

Plants are considered rich attractive sources for producing new bioactive compounds which exhibit a wide range of pharmacological activities. Family Aizoaceae is considered to be one of the South Africa largest succulent plant families, and it consists of four subfamilies named Sesuvioideae, Aizooideae, Ruschioideae, and Mesembryanthemoideae. Genus *Aptenia* consists of four species; *A. cordifolia, A. geniculiflora, A. haeckeliana,* and *A. lancifolia,* Besides *Aptenia* species are rich sources of natural metabolites from diverse chemical classes including oxyneolignans, flavonoids, sterols, lignans, amides and alkaloids with powerful anti-inflammatory activity. This review covers the literature until December 2018, providing a complete investigation of different isolated compounds from genus *Aptenia* with their available biological activities.

Key words

Aptenia, alkaloids, lignans, amides, anti-inflammatory

1. Introduction

Family Aizoaceae is considered to be one of the South Africa largest succulent plant and it constitutes a major part of the southern African succulent flora families [1], also few members of this family belonging to New Zealand and Australia [2] and it comprises 143 genera with about 2300 species [3]. "Mesembs" is a popular and well-known term for succulent members of the family Aizoaceae. These succulent members are sometimes placed in a separate family of their own, the Mesembryanthemaceae [4,5]. Four subfamilies are currently recognized in Aizoaceae, named Sesuvioideae, Aizooideae, Ruschioideae, and Mesembryanthemoideae. These were all shown to be monophyletic by means of chloroplast and nuclear markers [6].

Mesembryanthemoideae consists of about 100 species, and it is remarkable among the succulent Aizoaceae for its diversity of life and growth forms. There are annual and perennial herbs. Leafs and stems are succulents, geophytes, highly compact dwarf-shrubs while others are tall and woody shrubs that may exceed 1 m in height [7]. The leaves and stems are usually soft in texture and glistening or greyish-green in appearance. The glistening effect is due to the presence of prominent water-containing bladder cells [4].

Genus *Aptenia* is derived from the Greek word apten, meaning wingless, and this refers to the wingless fruit capsules of plants of this genus, and it belongs to the subfamily Mesembryanthemoideae [4]. As previously mentioned, four species of *Aptenia* are currently recognized as *A. cordifolia* (L.f.) Schwantes, *A. geniculiflora* (L.) Bittrich ex Gerbaulet, *A. haeckeliana* (A. Berger) Bittrich ex Gerbaulet, and *A. lancifolia* (L. Bolus) [7]. *A. cordifolia* received attention more than the other *Aptenia* species as Various classes of compounds have been separated from *A. cordifolia* like sterols, flavonoids, oxyneolignans, and alkaloids, whereas only alkaloids have been identified in *A. lancifolia* so far.

2. Phytochemical review

Many classes of secondary metabolites have been isolated from genus *Aptenia,* as follows:

2.1. Sterols

Sitosterol (**1**) and stigmasterol (**2**) were isolated from ethanol extract of the aerial part of *A. cordifolia* [8] **(Figure 1)**.

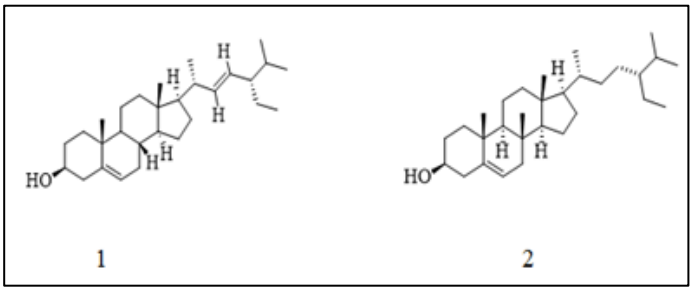

Figure 1: Chemical structure of sterol compounds **(1-2)**.

2.2. Flavonoids

Flavonoids are reported as powerful anti-oxidant compounds. Two flavanone glycosides, namely liquiritin (**3**) and naringenin (**4**), together with one flavonol glycoside (3`, 4`-dihydroxy-7-methoxyflavonol-3-O-*β*-D-glucoside) (**5**) were isolated from the aerial part of *A. cordifolia* [8] **(Figure 2).**

2.3. Lignans

Lignans are phenyl propanoid dimers found widely throughout the plant kingdom. They were reported to have remarkable

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antimicrobial and antiviral activities [9]. Cancer protective effect of dietary lignans have been also proved [10]. Oxyneolignan are dihydrophenyl propanoids acid units and the C_6-C_3 units are linked by an oxygen atom at C_4-$C_{4'}$ or C_4-$C_{2'}$. Six novel oxyneolignans [11], Apteniol A (**6**), Apteniol B (**7**), Apteniol C (**8**), Apteniol D (**9**), Apteniol E (**10**) and Apteniol F (**11**) and the new tetranoroxyneolignan [12], Apteniol G (**12**), were obtained from the leaves extract of *A. cordifolia* **(Figure 3)**.

Pinoresinol (**13**), syringaresinol (**14**), and (di-*erythro*-syringylglycerol-β-O-4,4`-syringaresinol ether) (**15**) are compounds contain lignan skeleton and isolated from alcoholic extract of *A. cordifolia* leaves [12] **(Figure 4)**.

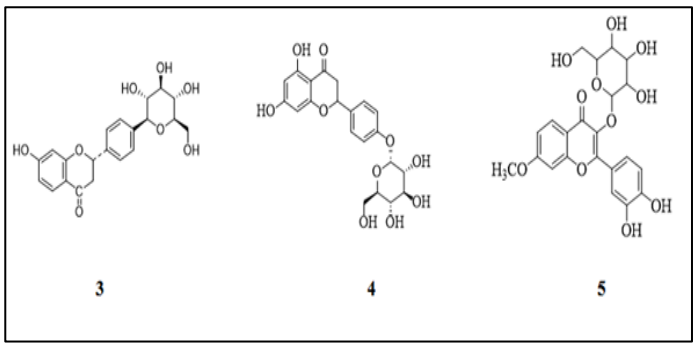

Figure 2: Chemical structure of flavonoidal compounds **(3-5)**.

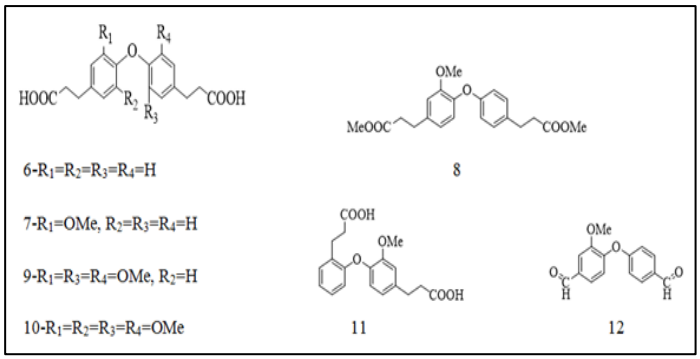

Figure 3: Chemical structure of compounds **(6-12)**.

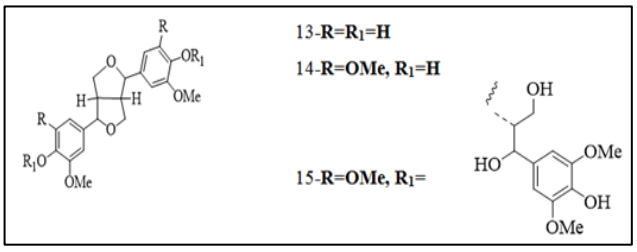

Figure 4: Chemical structure of compounds **(13-15)**.

2.4. Phenolic compounds

Phenolic and phenolic acid compounds were isolated from the alcoholic infusion of the fresh leaves of *A. cordifolia*, namely, 3,4,5-trimethoxyphenol (**16**), 4-hydroxybenzoic acid (**17**), methyl2,5-dihydroxybenzoate (**18**), 4-(hydroxylmethyl) phenol (**19**), and 4-(hydroxymethyl)-2,6-dimethoxyphenol (**20**) [12] **(Figure 5)**.

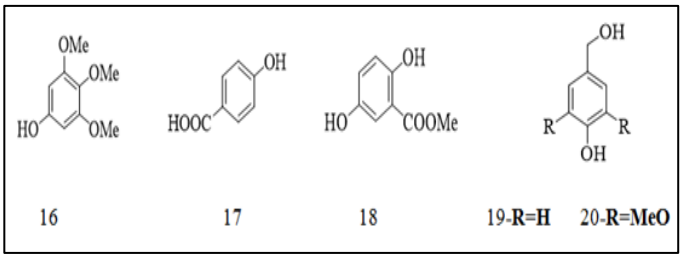

Figure 5: Chemical structure of phenolic compounds **(16-20)**.

2.5. Cinnamic acids derivatives

Acids along with their methyl and ethyl ester were identified from the leaves extract of *A.cordifolia*, namely, ferulic acid (**21**), methylferulate (**22**), sinapic acid (**23**), 3,4,5-trimethoxycinnamic acid (**24**), dihydrocinnamic acid (**25**), 4-hydroxy-dihydrocinnamic acid (**26**), dihydroferulic acid (**27**), 3,4-dimethoxy-dihydrocinnamic acid (**28**), 3,4-dimethoxy-dihydrocinnamic acid methyl ester (**29**), and 3,4-dimethoxy-dihydrocinnamic acid ethyl ester (**30**) [12] **(Figure 6)**.

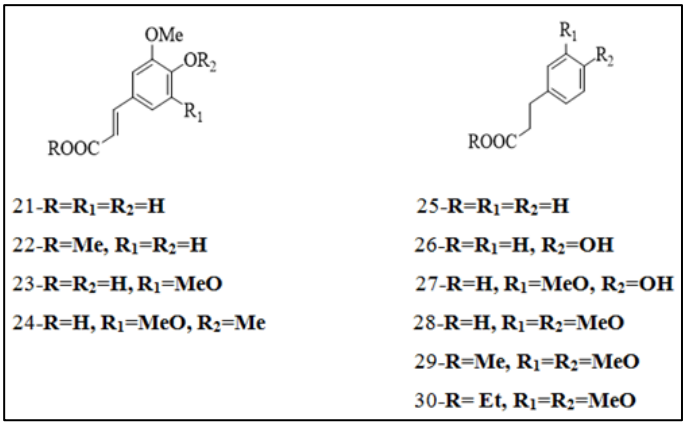

Figure 6: Chemical structure of cinnamic acid derivatives **(21-30)**.

2.6. Nitrogenous compounds

2.6.1. Alkaloids

Alkaloids are considered one of the most biologically active compounds. The race appears to be on finding new pharmacological functions as well as new plant sources for these compounds especially those who belonging to the family Aizoaceae (mesembrine type alkaloid) [13]. However, it has been reported that *A. cordifolia* was positive in general alkaloidal tests [14], a few number of alkaloidal components have been separated from this genus, such as, 2-(dimethylamino)-1-phenylethan-1-ol **(31)** [11], 3-(1H-indol-3-yl) propanoic acid (**32**) and methyl 3-(1H-indol-3-yl) propanoate (**33**) [12].

Chemical investigations of the extract provided from stems and roots of *A. cordifolia* revealed the presence of the mesembrine-type alkaloids, 4'-O-methylsceletenone (**34**) and [4,5] dihydro-4'-O-methylsceletenone (**35**) . On the other hand, the non-mesembrine alkaloid hordenine (**36**) was obtained from stems, roots, fruits, flowers and leaves of *A. lancifolia* , as well as stems of *A. cordifolia* [15] **(Figure 7)**.

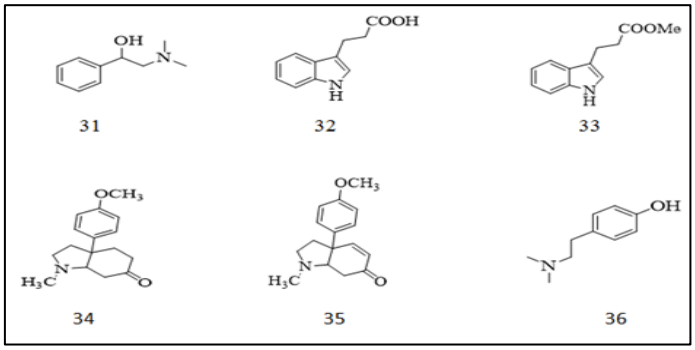

Figure 7: Chemical structure of alkaloidal compounds **(31-36)**.

2.6.2. Amides

Some of these compounds were isolated from the virus-infected tobacco leaves and it was suggested that they have antiviral effect. Ethanol extract of the leaves of *A. cordifolia* has produced five amide compounds (2S,*E*)-*N*-(2-Hydroxy-2-(4-hydroxyphenyl)ethyl) ferulamide (**37**), (*E*)-*N*-(2-Hydroxy-2-(4-Hydroxy-3-methoxyphenyl)-ethyl) ferulamide (**38**), (*E*)-*N*-(2-(4-Hydroxyphenyl)-2-propoxyethyl) ferulamide (**39**), (*E*,*E*)-*N*,*N*-Dityramin-4,4`-dihydroxy-3,5`-dimethoxy-*β*,3`-bicinnamamide (**40**), and 7-Hydroxy-1-(4-hydroxy-3-methoxyphenyl)-N_2,N_3-bis(4-hydroxyphenyl)-6-methoxy-1,2-dihydronaphthalene-2,3-dicarboxamide (**41**) [16] **(Figure 8)**.

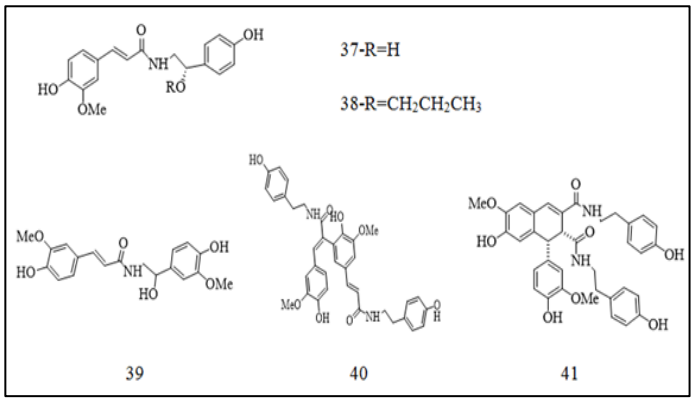

Figure 8: Chemical structure of amide compounds **(37-41)**.

2.7. Megastigmans and miscellaneous compounds

Norisoprenoids compounds were identified in the ethanol extract of *A. cordifolia* leaves, such as, 3-hydroxy-7,8-dihydro-*β*-ionone (**42**), (9R)-9-hydroxymegastigm-4-ene-3-one (**43**) ,megastigm-4-ene-3,9dione (**44**), dehydrololiolide (**45**), 4-oxo-7,8-dihydro-*β*-ionone (**46**), and (3R,9R)-3,9-dihydromegastigm-5-en-4-one (**47**) [12]. The compound 3-O-methyl-*chiro*-inositol (**48**) was also separated from the leaves extract of *A. cordifolia* [11] **(Figure 9)**.

3. Biological review

Few studies have been carried out to investigate the biological activity of *Aptenia*.

3.1. Anti-inflammatory activity

In a study by Waweru WR *et al.*, the anti-inflammatory activity of the ethanol extract of *A. cordifolia* was processed by using freshly prepared egg albumin (1% in normal saline**)** which was injected into the sub plantar tissue of the right hind paw of the rats. Wistar Albino rats weighing (110-220 g) were divided into four groups of six animals each. Group I served as the negative control and received 10 ml/Kg of distilled water orally. Group II was the positive control and received the reference drug diclofenac sodium 20 mg/Kg. Group III and IV received 150 mg/kg and 300 mg/kg of ethanol extract of *A. cordifolia*, respectively. Indication of inflammation was done by measuring the thickness of the right hind paws by a micrometer screw gauge. Paw size was measured at 0 hour, 1 hour, 2 hours, and 3 hours of egg albumin administration. The average size of each group was determined and compared with the negative and positive control. It was found that the ethanol extract of *A. cordifolia* leaf has powerful anti-inflammatory activity. The higher dose 300 mg/kg will inhibit inflammation after one hour, while lower dose 150 mg/kg shows anti-inflammatory activity after two hours of inflammation induction [17].

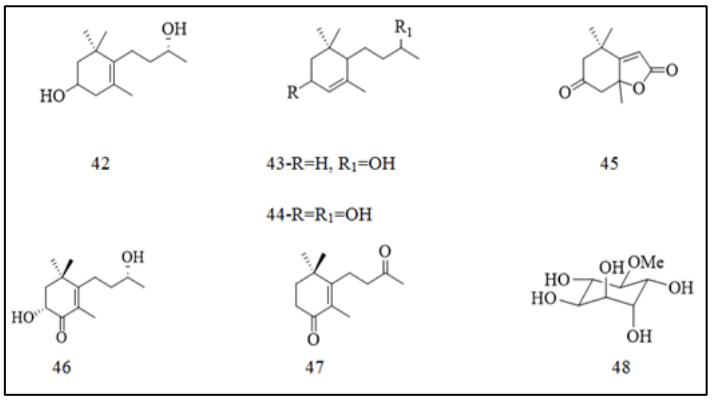

Figure 9: Chemical structure of megastigmans and miscellaneous compounds **(42-48)**.

3.2. Schistosomicidal activity

A stock solution (10 mg/mL) of methanol extract of *A. cordifolia* shoot system was diluted with RPMI (culture medium) to produce 3 mL test solution of 100 µg/mL final concentration in a 10 mL vial for the screening. Three replicates were used for the extract, and three pairs of worms (males and females equally represented) were placed in each vial using sterilized tissue forceps. Incubation was maintained at 37 ^{0}C. Positive (praziquantel, at 0.1 µg/mL) and negative (DMSO) controls were simultaneously applied. Examination for worm viability was done after 24 hrs using a stereomicroscope. Worms showing no signs of motility for 1 min were considered dead. The activity of the extract was measured by calculating the number of dead worms relative to the total number of worms. The literature surveyed that *A. cordifolia* showed no Schistosomicidal activity [18].

4. Conclusion

A. cordifolia has received the most attention among the various *Aptenia* species. With further research, other species may also

prove to be suitable candidates for drug development. There are different classes of compounds that have been separated from *A. cordifolia* like sterols, acids, alkaloids, oxyneolignans, lignans, and amides. *A. cordifolia* showed powerful anti-inflammatory activity and negative Schistosomicidal effect. It is hoped that further phytochemical investigations on *Aptenia* species and considerable biological studies on different species, total extracts, different fractions, and also on isolated pure compounds will be done in the future to reveal the importance of this genus.

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