Journal of Pharmacognosy and Phytochemistry

Available online at www.phytojournal.com

J P P Journal of Pharmacognosy and Phytochemistry

ISSN 2278-4136
JPP 2014; 3 (2): 147-157
Received: 21-05-2014
Accepted: 12-06-2014

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Some rare Tanzanian plant species as sources of less common metabolites: biomedical potential and conservation status

Stephen S. Nyandoro

Abstract
The paper presents a review on the biomedical potentials of less common natural products recently isolated from some rare plant species indigenous to Tanzania. The conservation status of the plant species under review is also discussed. Cinnamoyltetraketide derivatives, *pseudo*-nucleoside and aristolactams from *Toussaintia orientalis* (Annonaceae); heptenolides from *Cleistochlamys kirkii*, (Annonaceae); acetogenins, cyclitols and meroditerpenoid from *Artabotrys* species (Annonaceae); geranylbenzoquinonoids from *Lettowianthus stellatus* (Annonaceae); furanoditerpenoids from *Stuhlmania moavi* (Caesalpiniaceae); *nor*-halimanoid and *ent*-clerodanoid diterpenes, chlorobenzenoid, and other metabolites from *Tessmannia* species (Caesalpiniaceae) are some of those covered in this review.

Keywords: Cinnamoyltetraketide derivatives, *pseudo*-nucleoside, aristolactams, heptenolides, cyclitols, acetogenins, geranylbenzoquinoids, diterpenoids; Annonaceae, Caesalpiniaceae.

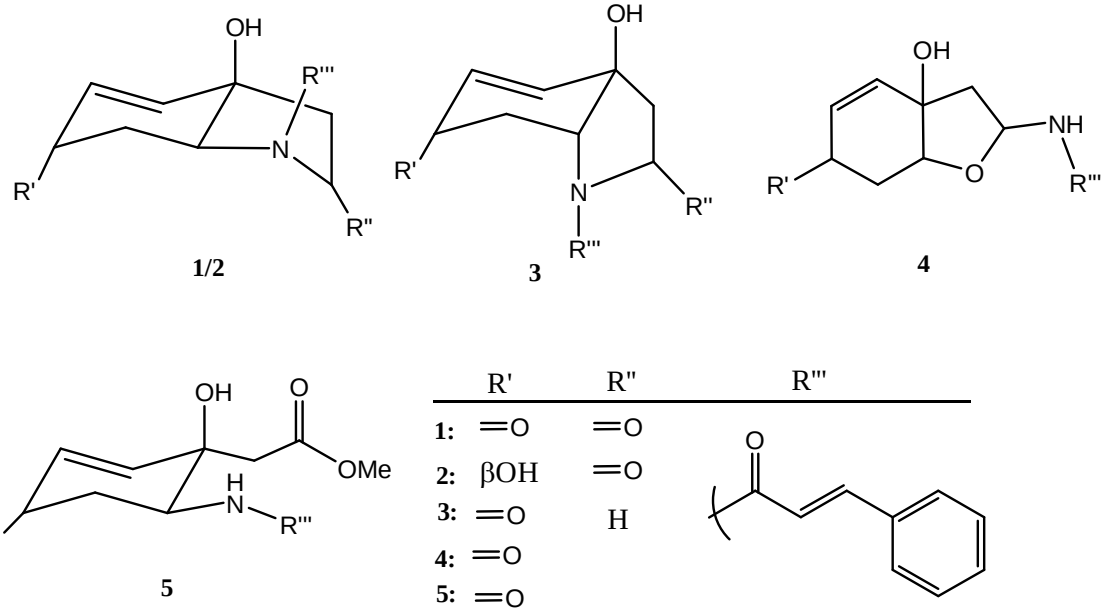
1. Introduction

Tanzania is among the group of African countries with the highest levels of biodiversity, with an estimated 11,000 species of vascular plants, which is approximately 37% of the plant species of tropical Africa [1]. The Tanzanian floral diversity is concentrated in its biodiversity hotspots comprising of the Coastal and Eastern Arc Mountain Forests that occupy less than 5% of its total land area of 885,800 km² [1]. This ecological region globally ranked as tenth for its biodiversity importance, is not only known for its high level of species richness, but also as a center of floral endemism, with approximately 1,200 higher plant species so far reported to occur exclusively in Tanzania [2-6]. Although numerous plant species are traditionally used for the treatment of various ailments and for other health care needs, such endemic and rare plant species growing in Tanzania may not be utilized as herbal remedies, probably due to their non-conspicuousness. As such, many of them have normally not been considered for phytochemical investigations for bioactive metabolites. However, some of the rare plant species that have been studied have revealed a number of unique compounds, several of which also possess potent biomedical activities [7, 8]. Conversely, though the Tanzanian population density is not significantly higher than in many African countries, its inhabitants are mainly concentrated in the areas with the highest numbers of rare and endangered plant species, which include parts of the afore-mentioned hotspots [1], thus creating a conservation concern for sustainable utilization. In this context, *Toussaintia orientalis*, *Cleistochlamys kirkii*, some *Artabotrys* species, and *Lettowianthus stellatus* which are among the rare plant species from the family Annonaceae, as well as *Stuhlmania moavi* and *Tessmannia* species from the family Caesalpiniaceae, were recently included in the phytochemical investigations carried out in the Chemistry Department, University of Dares Salaam, in order to unravel their bio-medically active and other constituents, the outcome and their conservation status of which is reviewed in this paper.

2. Cinnamoyltetraketide derivatives, *pseudo*-nucleoside and aristolactams from *Toussaintia orientalis*

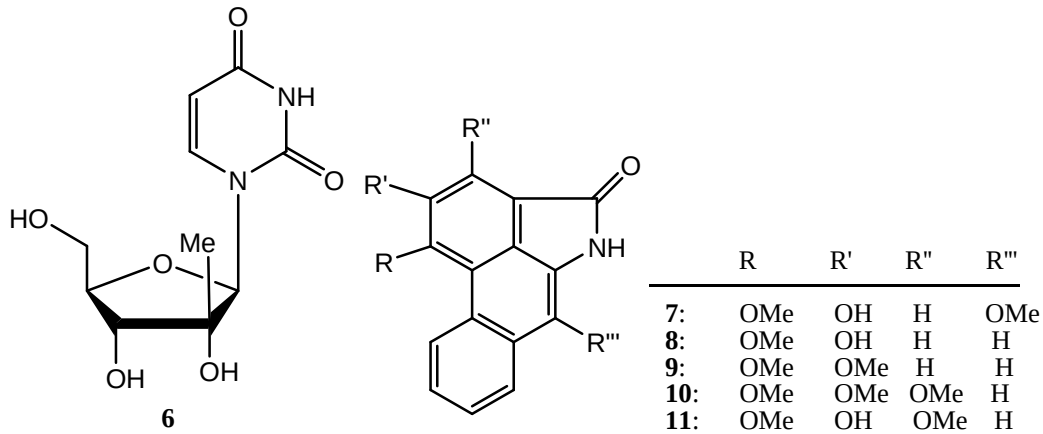
Phytochemical investigations of the leaf extracts from *Toussaintia orientalis* Verdc. yielded novel antimicrobial cinnamoyltetraketide derivatives, namely toussaintine A – E (**1-5**), together

with other metabolites [9]. These newly discovered nitrogenous natural products are conceivable metabolites of a parent tetraketide whose cyclization processes would determine the type of structural framework of the compounds found in *T. orientalis* leaves. Thus, the tetraketide could undergo cyclization leading to the formation of an indolidinoid (**1-3**), hydrobenzofuranoid (**4**) or cyclohexenoid (**5**) ring coupled to a cinnamamide moiety that would be formed through the shikimic acid pathway [9].



Isolation of the cinnamoyltetraketide derivatives **1-5** from *T. orientalis* is interesting both from a structural and biomedical point of view as these compounds contain α,β-unsaturated amido and ketonic carbonyl groups that are expected to be of significance for their reported antimicrobial efficacy corroborating previous studies [10, 11]. This was the first time that indolidinoids of the general structure displayed by compounds **1** – **3**, as well as the other compounds **4** and **5**, have been isolated from natural sources, hence indicating the significance of the rare Tanzanian Annonaceae species as potential sources of unusual natural products.

Phytochemical investigations of the root and stem bark extracts of *T. orientalis* yielded the *pseudo*-nucleoside 1-(2-methyl-β-D-ribofuranosyl)-uracil (**6**), a new aristolactam alkaloid namely aristolactam AIV (toussalactam, **7**), the known aristolactams aristolactam AII (**8**), aristolactam BII (cepharone B, **9**), piperolactam C (**10**) and aristolactam FII (godiopeladine, **11**); together with several other metabolites [12, 13]. The ariolactams exhibited antimicrobial, cytotoxic and anti-inflammatory activities, with aristolactam FII (**11**) showing activity close to that of the standard anti-inflammatory agent Indomethacin and cytotoxic drug Camptothecin. The compounds also exhibited either mild or no antiproliferative activity [12].



	R	R'	R''	R'''
7:	OMe	OH	H	OMe
8:	OMe	OH	H	H
9:	OMe	OMe	H	H
10:	OMe	OMe	OMe	H
11:	OMe	OH	OMe	H

This was the first time for the isolation of the *pseudo*-nucleoside **6** from a plant source, previously being reported as a synthetic product [14], while other similar compounds are reported from marine sponges [15, 16]. Although the nucleoside **6** exhibited weak antimicrobial, cytotoxic, anti-inflammatory and anti-proliferative activities, its similar compounds are

known as antiviral agents and several efforts have been made to obtain such compounds through chemical synthesis. The resulting synthetic products when evaluated for antiviral potency showed remarkable activity [14]. Since synthetic strategies reported for nucleoside are quite tedious and resulted into poor yield [14], *T. orientalis* might be an interesting natural and renewable source of this bio-medically important molecule.

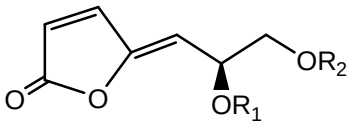
Aristolactum alkaloids similar to compounds **7 - 11** previously obtained from other sources are reported to possess cytotoxicity against HeLa cell line (human cervical carcinoma), antiproliferative activity against human chronic myeloid leukaemia (K-562) and mouse fibroblast (L-929) cell lines [17]. Several other aristolactams have been shown to possess cytotoxicity, antibacterial, antimalarial, platelet aggregation activities and other physiological properties [18-20]. Such a broad biomedical activity indicates the aristolactam skeletal framework and its substituents to play an important role that deserves further bio-prospecting efforts for these natural products as lead compounds in drug development.

T. orientalis is one of four species of the genus *Toussaintia*, which is exclusively found in Africa. Other species are *T. congolensis* Boutique (type species) growing in Congo, *T. hallei* Le Thomas found in Gabon, and *T. patriciae* Q. Luke & Deroin which is endemic to Tanzania [2, 21]. None of the four *Toussaintia* species has been comprehensively investigated for chemical constituents, apart from the recent studies on the Tanzanian species. *T. orientalis,* locally known as 'Msofu Simba' (a name given to several Annonaceae species) in Tanzania is used as an herbal remedy for the treatment of various illnesses. Thus, its roots mixed with lion skin and then boiled to produce a concoction is taken for the treatment of asthma and skin rashes arising from abdominal worms. The leaves of this plant when mixed with chicken feathers are burnt and the resulting ashes after mixing with coconut oil are used as a topical treatment of irritating rashes [9].

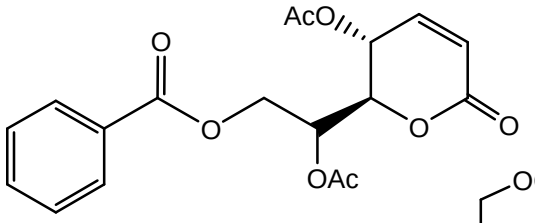
In Tanzania, *T. orientalis* occurs in few localities with limited distribution within the coastal forests, including Zaraninge Forest Reserve (currently part of Saadani National Park), Pugu and Banda forests in Coast Region, and from the Eastern Arc Mountains near Ifakara in Kilombero District [21]. It is considered vulnerable to extinction and is among those endangered plant recorded in the red list of threatened floral species [2, 22, 23]. It has almost certainly gone extinct in Kenya, where it was once collected nearby Mangea. In Tanzania it can still be found in fragmented patches at the coastal forests where it is under severe threat of extinction. The plant cannot be found in Pugu Forest, and probably around Ifakara in the Kilombero river valley and Ruvu South Forest Reserve anymore, which used to be localities for its habitats [2, 21-23]. Therefore, this alarming biodiversity threat requires further conservation action in order to protect this valuable bio-resource.

3. Heptenolides from *Cleistochlamys kirkii*

Recent phytochemical investigations of the fruits and stem bark extracts of *Cleistochlamys kirkii* Benth (Oliv.) yielded the heptenolides (+)-melodorinol (**12**), (+)-acetylmelodorinol (**13**), (+)-sphaerodiol (**14**), (+)-benzoylmelodorinol (**15**), and (-)-cleistenolide (**16**). Phytochemical studies of the leaves yielded compounds **12**, **13** and **16,** together with the cyclohexene derivatives (-)-cleistodienol (**17**) and 1,6-desoxy-β-senepoxide (**18**) [24]. The two recently isolated plant constituents (**16**) and (**17**), together with heptenolides **12** - **15** exhibited activity against *Staphylococcus aureus* and *Bacillus anthracis*, antifungal activity against *Candida albicans*, and cytotoxicity in the brine shrimp (*Artemia salina*) larvae leathality test [24]. The antibacterial activity demonstrated by these compounds and the extracts they were extracted from validated the traditional use of the plant extracts for ailments related to bacterial infections, thus indicating that *C. kirkii* is a bio-resource warranting further scientific enquiries.



12: R_1 = H, R_2 = COPh
13: R_1 = COMe, R_2 = COPh
14: R_1 = R_2 = H
15: R_1 = R_2 = COPh



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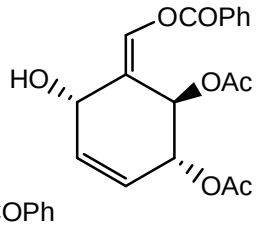

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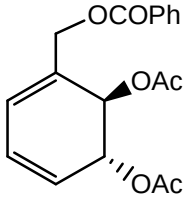

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The heptenolides **12** - **15** that have antitumor and/or other biological activities were previously obtained from either South East Asian or Tanzanian *Sphaerocoryne* (*Melodorum*) species [25-27]. More recently, another Annonnaceae species endemic to Tanzania, *Uvaria lungonyana* collected from the Lungonya River Valley in the Selous Game Reserve, yielded the heptenolides **12** and **13**, where compound **12** exhibited larvicidal efficacies against *An. gambiae* mosquito larvae and antimicrobial activity [28]. Due to their biomedical potential, such heptenolides attracted attention of synthetic chemists soon after their discovery in the early 1990s. Most of these compounds exhibit significant cytotoxicity against several tumor cell lines, but were not yet advanced to clinical applications due to their non-selectivity [29]. The bioactivities demonstrated by these plant constituents suggest their potential applications as biomedical agents once their setbacks are addressed.

The recently discovered antimicrobial heptenolide (**16**) has also been synthesized by a number of research groups to produce larger amounts of the metabolite for biomedical

applications [30-33]. However, all synthetic strategies reported so far are inefficient. Therefore, the option to obtain this compound from natural sources upon optimization of its production is an attractive endeavour, particularly since the compound is found in the easily renewable plant part, i.e. the leaves.

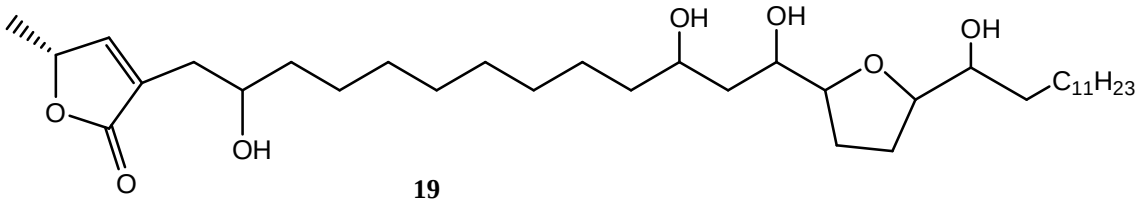
Cleistochlamys kirkii is a single species of the genus *Cleistochlamys* belonging to the family Annonaceae. The genus is among the six near-endemic genera found in coastal Tanzania. Its occurrence extends to northern Mozambique [34] and eastern Malawi, Zambia and Zimbabwe [35], the locations being regarded as extensions of the East African Coastal and Eastern Arc Mountain vegetation belt extending to southern, southwest and beyond Tanzania [36]. In Tanzania, the plant species is found in Weme Forest Reserve, in the Rufiji flood plain, and recently collected from the eastern edge of the Namatimbili Hill of Mchakama village, Kilwa district in Lindi region. No ethnomedical use of this plant is documented in Tanzania. However, in Mozambique, an extract of the plant is used in the treatment of haemorrhoid wounds, rheumatism and tuberculosis [24, 34].

The genus *Cleistochlamys* is among the rare plant species consisting of such less common plant constituents as **12 - 18**. Although there is no IUCN assessment recorded so far for this plant, its restricted distribution and a number of threats, including expanding agriculture, increased land demand for human settlements and logging for charcoal production in the localities where it grows in Tanzania warrants immediate conservation action to be undertaken.

4. Acetogenins, cyclitols and meroditerpenoid from *Artabotrys* species

Recently, *Artabotrys* species growing in Tanzania were included as among the target plants for the on-going phytochemical investigations of Tanzanian Annonaceae species. Initial investigations yielded the antibacterial and antifungal tetrahydroxylated monohydrofuranyl acetogenin (**19**) and the cyclitol L-quebrachitol (**20**), among other constituents from the root barks of *Artabotrys brachypetalus* [37, 38], a plant used as a remedy for the treatment of gonorrhea [39]. Due to the diverse bioactivities of the previously reported annonaceous acetogenins [40] and the medicinal potencies of cyclitols [41], these initial results prompted further investigations of similar metabolites from other *Artabotrys* species occurring in Tanzania. Included in the further investigations was *A. modestus* spp *modestus*, a plant species whose leaf infusion is taken as a remedy for nausea and vomiting, while a concoction of its root barks is used against stomachache and diarrhea [42]. Thus, investigations of the petroleum ether extract of the stem bark of *A. modestus* spp *modestus* afforded the antifungal acetogenin derivative β-methoxy-γ-methylene-α,β-unsaturated-γ-butyrolactone (artapetalin B, **21**) together with other metabolites [43]. The antifungal effectiveness of artapetalin B (**21**) against *C. albicans* was ascribed to the presence the butyrolactone moiety [43], a characteristic component of a large number of biologically active natural products [44].

Artapetalin B (**21**) was previously isolated together with its derivatives from *A. hexapetalus* [45]. Although many secondary metabolites are known to contain the butyrolactone ring, the isolation of compound **21** with the unusual β-methoxy-γ-metheylene-substituted α,β-unsaturated-γ-butyrolactones functional group is a rare phenomenon. It is of chemotaxonomic significance since the compound was recorded for the second time from plant species of the genus *Artabotrys*, showing phylogenetic relationship between *A. hexapetalus* and *A. modestus* spp *modestus*. Furthermore, this was the third time for an Annonaceous acetogenin and/or their derivatives to be obtained from the genus *Artabotrys*.



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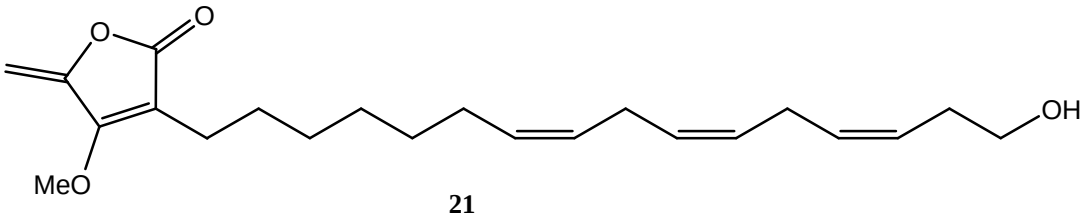


21

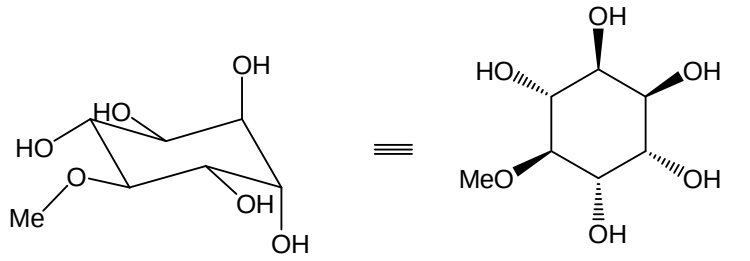
Generally, acetogenins and compounds having a butyrolactone moiety such as artapetalin B (**21**) are known to possess biological properties including insecticidal and antiviral activities [46]. Although not generally used for pest control, several species of the family Annonaceae have been established to possess insecticidal and antitumor activity, which in most cases is ascribed to the constituent acetogenins that are restricted to this family [46]. Thus, Annonaceae species have been targeted as potential sources of naturally occurring insecticides and antitumor agents, of which *Artabotrys* species would offer an alternative bio-resource for these bio-medically important plant metabolites.

Phytochemical investigations of the ethanol extract of the stem bark of *Artabotrys modestus* Diels ssp *macranthus* Verdc. yielded the antibacterial cyclitols quebrachitol (**20**) and cyclohexane-1,2,4,5-tetrol (**22**), the former having been previously obtained from *A. brachypetalus* [38, 43]. Cyclitols, sometimes also called inositols, which means sugar-alcohols,

are cycloalkanes containing one hydroxyl group on each of their three or more ring atoms. These alicyclic polyhydroxy compounds are considered to be a special class of carbohydrates which occur in nature [47]. One of the roles of these exclusively plant metabolites is to help plants to survive adverse environmental conditions. Quebrachitol [L-(-)-2-*O*-methyl-*chiro*-inositol] (**20**) is reported to occur in high concentration in the serum of the stem barks of the rubber tree (*Hevea brasiliensis*) and can conveniently be isolated from the rubber latex waste liquor [48]. Several biologically active compounds, including their derivatives such as other inositols, L- and *pseudo*-monossaccharides, aminoglycoside- and aminocyclitol-based antibiotics and compounds functioning as enzyme inhibitors, have been synthesized from quebrachitol [49]. On the other hand, D-pinitol (3-*O*-methyl-D-*chiro*-inositol, **23**), which is a stereoisomer of L-quebrachitol (**20**) found to accumulate in many plant species during periods of elevated temperatures and in drought conditions, has been widely studied for its physiological properties [50]. Because of its medicinal importance as a hypoglycemic agent [51], D-pinitol has been patented for its ability to alleviate symptoms associated with diabetes. Many physicians regard D-pinitol as one of the best insulin mimicks [52].

The isolation of tetrol **22** from *Artabotrys modestus* ssp *macranthus* is its first record of occurrence from plant sources, yet it was previously isolated from marine algae [53, 54] and recently synthesized in racemic form [55]. Tetrol **22** belongs to the class of cyclohexanetetrol isomers of which only three were so far isolated from nature [56]. These include betitol whose structure and occurrence remains uncertain, and was reported to be present in trace amounts in sugarbeet molasses [57, 58], D-(+)-1,2,4,5-cyclohexanetetrol [53, 54] and toxacarol [1,2,3,4-cyclohexanetetrol] isolated from the plant species *Toxocarpus himalensis* [59].

Cyclitols such as **20**, **22** and **23** are considered to be potentially versatile chiral building blocks in natural and semi-synthetic bioactive products. The cyclic structures of cyclitols allow the regio- and stereo-selective introduction of a variety of functionalities on the ring(s). By subsequent cleavage of the cyclohexane ring at particular positions, cyclitols have been used as precursors of both acyclic and heterocyclic compounds [49]. Therefore, the isolation of cyclitols **20** and **22** from *A. modestus* ssp. *macranthus* has provided a new natural source of these versatile building blocks in the construction of bioactive compounds, being a significance contribution towards biomedical research.



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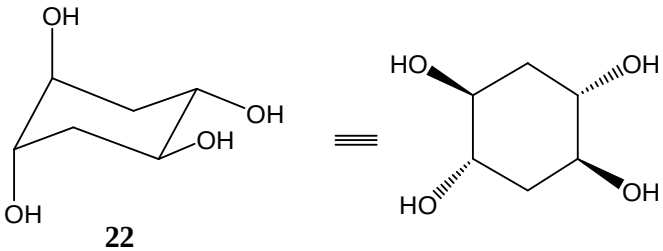

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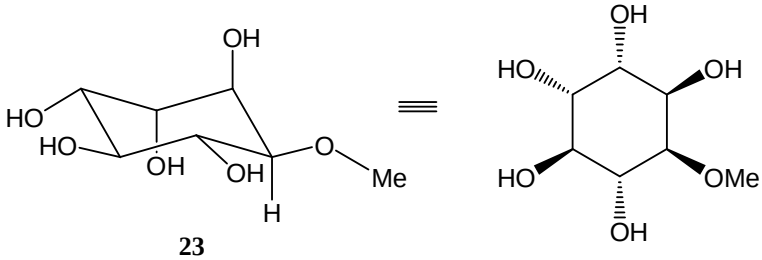
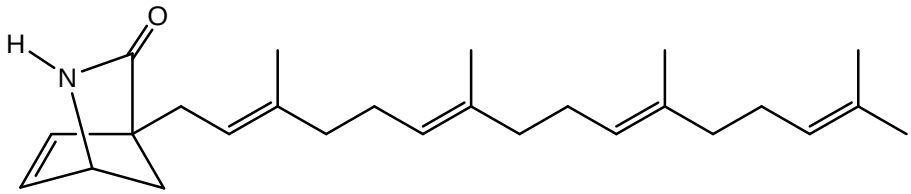


23

A novel meroterpenoid {1-[(2*E*,6*E*,10*E*)-3,7,11,15-tetramethylhexadeca-2,6,10,14-tetraenyl]-2-azabicyclo[2.2.1]-hept-5-en-3-one} named artabotramide (**24**), was obtained from the petroleum ether extract of the root barks of *A. modestus* ssp *macranthus* together with other known metabolites. The metabolite, which is a conceivable alicyclic diterpene attached to a bicyclic triketide that incorporates an amino moiety, exhibited larvicidal activity against *A. gambiae* s.s Giles mosquito larvae [43]. There is no natural product having a 2-azabicyclo[2.2.1]hept-5-en-3-one (ABH) moiety previously reported in the literature.

Structurally and from the biomedical point of view the isolation of artabotramide (**24**) is interesting, since this compound contains an amide moiety which could be a pharmacophore portraying potent drug action. Furthermore, the 2-azabicyclo[2.2.1]-hept-5-en-3-one (ABH) moiety present in compound **24** is of medicinal potential, being one of the target pharmacophores in the synthesis of anti-retroviral

carbocyclic nucleoside analogues such as (±)-carbovir and abacavir [60-63]. Therefore, artabotramide (**24**) is a potential resource for further investigations as a lead compound for the development of pharmaceutical carbocyclic nucleosides. The metabolite could as well be considered as a new lead for the development of larvicidal or insecticidal agents. Thus, the unprecedented isolation of artabotramide from *A. modestus* ssp *macranthus* suggests the plant species to be a potential bio-resource for further investigation for carbocyclics that are potentially important in biomedical research.



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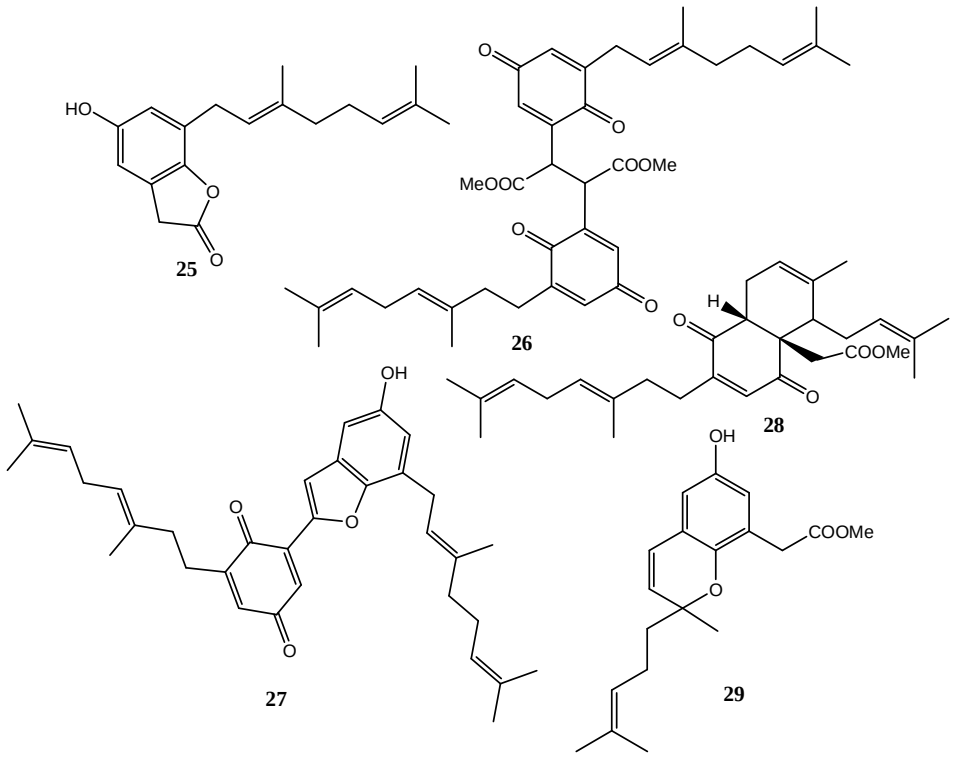
The genus *Artabotrys* (commonly known as Tail Grape) is among the relatively large genera of the family Annonaceae, consisting of at least 100 species which are distributed in Africa and East Asia [21]. *A. brachypetalus* and *A. modestus* are among the seven species recognized in Tanzania. So far there is no IUCN evaluation recorded to establish the conservation status for *A. brachypetalus*. The species grows in southeastern Tanzania, Central and South African countries [64]. While *A. modestus* spp *macranthus*, a plant native to Kenya and Tanzania coastal forests, has been categorized as of least concern by IUCN [65], *A. modestus* spp *modestus*, which is an endemic species to Tanzania, is considered as critically endangered [66]. The latter species is so far reported to be confined to Rondo Forest Reserve and Noto Plateau in the Lindi Rural District [66] and a patch of bush near Masurungu Village along the Bagamoyo-Msata road in Bagamoyo District of Tanzania [43]. In fact it might as well have already been cleared from the latter location due to the on-going road expansion works.

5. Geranylbenzoquinonoids from *Lettowianthus stellatus*

Phytochemical investigations of the fruits of *Lettowianthus stellatus* Diels for bioactive metabolites yielded variously substituted geranylbenzoquinonoids, namely lettowienolide (**25**), lettowiquinone (**26**), lettowifuraquinone (**27**), lettowinone (**28**) and lettowipyraquinol (**29**), together with (*Z*)-7-octadecen-9-ynoic acid and juvenile hormone III [67]. Among the quinonoid derivatives reported from *L. stellatus*, only **25** and **26** were evaluated for antimalarial activity and exhibited mild activity (IC_{50} 20 mg/mL, each) [67].

Over 1200 naturally occurring quinones have been established to occur in both animals and plants, as pigments and as intermediates in cellular respiration and photosynthesis, a number of which possess anticancer and antileishmanial properties [68-70]. Thus, the isolation of the novel quinonoid derivatives from this rare Annonaceae plant further demonstrates the widespread occurrence of variably substituted quinones as natural products, some having unusual substitution frameworks.



25 **26** **27** **28** **29**

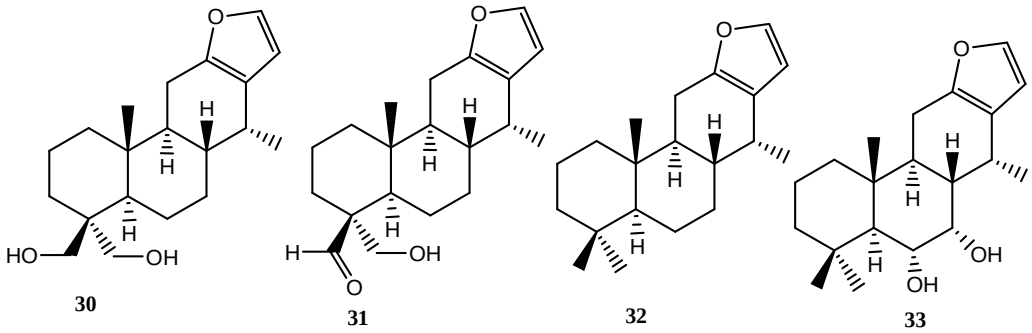
Lettowianthus stellatus is the only species of the genus *Lettowianthus* (Annonaceae) and it occurs in the biodiversity hot spots of the Coastal and Eastern Arc Mountain forests of Kenya and Tanzania [21,71]. No medicinal uses have been yet

reported for *L. stellatus*, but its edible fruits are used to make local wine [67]. The plant is considered as a vulnerable species with restricted occurrence to the remnant forest patches of the coastal forest in Southern Kenya and in Tanzanian coastal forest, extending inlands to the Eastern Arc Mountains [71]. In Tanzania, the plant is found in some forest reserves and other protected areas like Udzungwa National Park, thus ensuring its continued existence only in the restricted areas, as in the non-protected areas there are still threats arising from expanding agriculture, urbanization and logging for charcoal production [71].

6. Furanoditerpenoids from *Stuhlmania moavi*

In the search for bioactive constituents from the less common Tanzanian indigenous plant species, two new furanoditerpenoids (voucapenoids) **30** and **31**, together with other known voucapenoids **32** and **33**, were recently isolated as anti-proliferative, antibacterial, antifungal and cytotoxic constituents of the Tanzanian plant species *Stuhlmania moavi* Verdc. (Caesalpiniaceae) [72].

Furanoditerpenes belong to the class of diterpenoids characterized by a molecular skeleton formed through the fusion of three cyclohexane rings in a saturated phenanthrenoid carbacyclic system and a furan ring. Diterpenes of this kind are of limited occurrence, mostly being distributed in genera the *Caesalpinia* [73-75] and *Pterodon* [76]. Some members of this class of diterpenoids have been reported to show antiviral [73, 75], antimicrobial [65] and plant growth regulatory [76] properties. The compounds isolated from *S. moavi* exhibited anti-proliferative, cytotoxic, antibacterial and antifungal activities, with some of the results corroborating the medicinal uses of the crude extracts for the treatment of skin infections [72]. Thus, the isolation of furanoditerpenoids from *S. moavi* with diverse bioactivities indicated the importance of diverse structural functionalization of metabolites from such a natural source that can be tapped for biomedical applications.

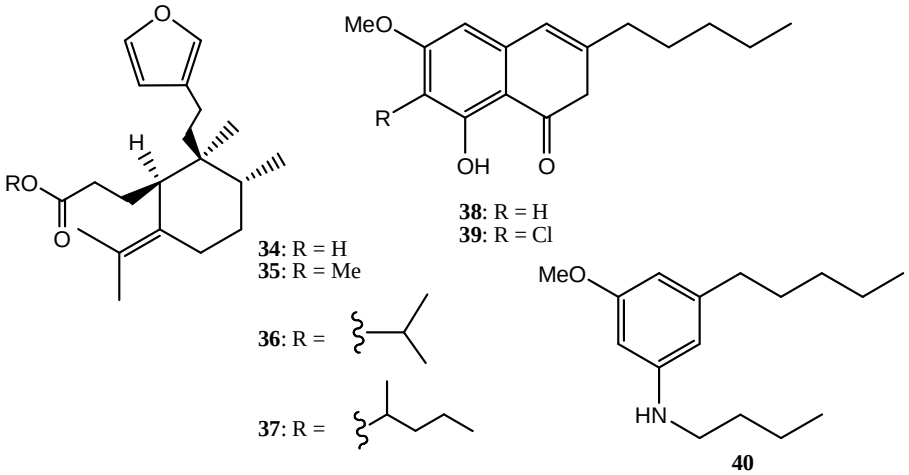


30 **31** **32** **33**

Stulhmania moavi Verdc. belongs to a monotypic genus *Stulmania* (Caesalpiniaceae). The plant species is endemic to Tanzania, occurring in the unprotected Kwedijela forest in Handeni District, Tanga Region [72]. Although no IUCN assessment is so far recorded for this plant, it can at least be categorized as vulnerable due to its limited distribution and to a number of threats including expanding agriculture, increased land demand for human settlements and logging for charcoal production in the localities where it grows (personal observations in the field).

7. *Nor*-halimanoid, *ent*-clerodanoid diterpenes, chlorobenzenoid and other metabolites from *Tessmannia* species

Recently, several Tanzanian plant species have been included in the on-going phytochemical investigations for plant-based antimosquito agents [28, 77-81]. Such studies led to the isolation of the *nor*-halimanoid diterpene tessmannic acid (**34**), its esters **35–37**, together with the unusual isocoumarins **38** and **39**, and 5-pentyl-3-methoxy-*N*-butylaniline (**40**) from *Tessmannia densiflora* Harms (Caesalpiniaceae). Tessmannic acid (**34**) and its methyl ester (**35**) exhibited antibacterial and antifungal activity. The compounds also caused high larvae and adult *Anopheles gambiae* mosquitoe mortality effects, and stronger mosquito repellency than that shown by the standard repellent DEET, hence indicating *Tessmannia* species to be potential sources of bioactive natural products [77].

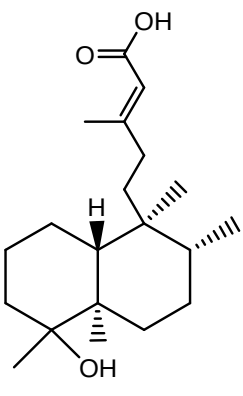


34: R = H
35: R = Me
36: R =
37: R =

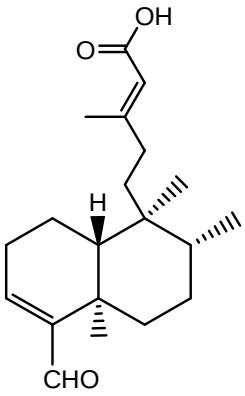
38: R = H
39: R = Cl

40

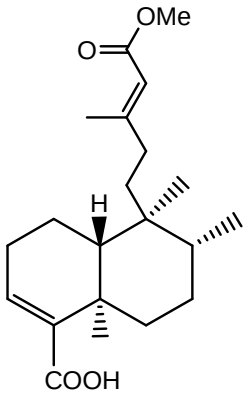
Phytochemical investigations of other Tanzanian *Tessmannia* species, namely *T. martiniana* var *pauloi* and *T. martiniana* var *martinianan* yielded the clerodane diterpenoids **41** and **42**, *ent*-clerodane diterpenoids **43**-**45**, and the chlorobenzenoid **46**.



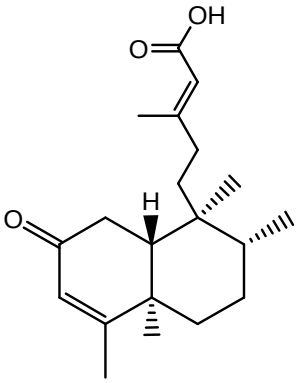
41



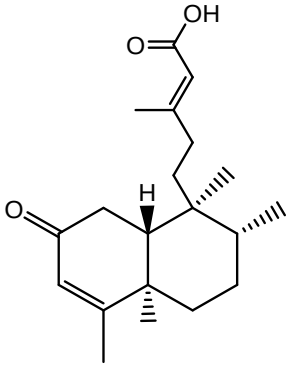
42



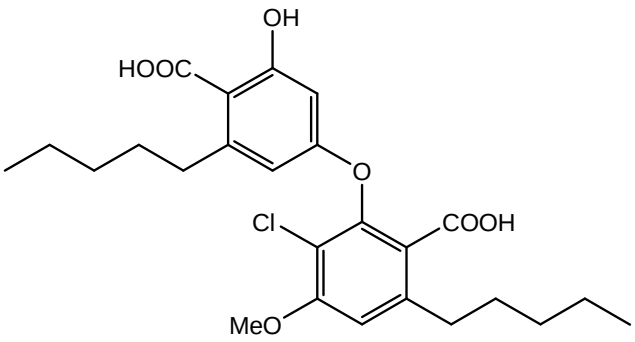
43



44



45



46

Some of the compounds and extracts containing them exhibited significant antimosquito, antifungal and antibacterial activities [78].

There are neither ethnomedical nor antimosquito uses reported for these Tanzanian *Tessmannia* species. Thus, the isolation of the bioactive compounds as stated above indicates *Tessmannia* species to be potential sources of bioactive natural products that could provide an alternative avenue of a varied class of metabolites for further development of plant-based antimosquito agents, whereas the crude extracts could also serve as larvicides in their own right in managing various mosquito habitats. Hence, further initiatives are needed to discover new lead compounds for the development of insecticidal and other biomedical agents from locally available plant resources.

Tessmannia is one of about 700 genera of the family Caesalpiniaceae consisting of 11 species that are mainly found in Central and West Africa [82, 83]. Three *Tessmannia* species (*T. densiflora* Harms, *T. martiniana* var *pauloi* Harms, *T. martiniana* var *martiniana* Harms and *T. burttii* Harms) are known to occur in Tanzania. The former two species are endemic to Tanzania while the latter can also be found in Zambia and the Democratic Republic of Congo [82, 84]. *T. martiniana* var *pauloi* and *T. martiniana* var *martiniana* grow in the coastal evergreen forest reserves of Pugu and Zaraninge in Kisarawe and Bagamoyo Districts, Coast Region of Tanzania, respectively. Unlike the latter reserve, the former is seriously degraded due to deforestation, charcoal production, farming activities and encroachment for settlement within the reserve, thus threatening the survival of the species therein despite various conservation initiatives [85]. There are no IUCN evaluation records available for the two varieties of *T. martiniana*. On the other hand, *T. densiflora*, which is listed as an endangered species by IUCN, is known from only two localities on the Matumbi and Kichi Hills of Rufiji District, Coastal Region. The two sites are not protected and are open to exploitation. Of particular concern are the logging of commercial species in the valleys and the potential level of encroachment of an increasing human population, thus posing an extinction threat if conservation actions are not taken in the near future [86].

8. Conclusion

The occurrence in rare plant species of less common metabolites, some with unusual structural frameworks as reviewed in this paper further supports the philosophy that plants are the reservoir of structurally diverse natural products, some of which possess biomedical potency. Therefore, since only a few of the plants found in the tropical environments have been investigated for this purpose, more efforts are still needed to investigate plant species, especially the rarely occurring ones, in order to unravel the full potential of untapped, hidden wealth of bioactive compounds needed for the pharmaceutical industry. Moreover, indigenous plant species of both established ethno-medical value as well as

those with scanty or non-recorded value should be evaluated for their bioactive metabolites to further contribute remedies for the ever-increasing health care needs.

Some of the plant species whose metabolites are covered in this review are among the extremely rare species that are endemic or near endemic to Tanzania. Because of their scarce occurrence and restricted distribution, the plant species are potentially vulnerable to extinction within an unpredictable future. Thus, the isolation of the metabolites, which have proved to be of pharmacologic value from such plants, underscores once again the need for conservation of biodiversity for sustainable utilization and development of the genetic resources.

9. Acknowledgements

Author extends his appreciations to Prof. Nkunya MHH, the former leader of the Natural Products Research Group in the Chemistry Department, University of Dar es Salaam, his co-workers and students, in particular Drs. Makangara JJ, Kihampa C and Odalo JO whose original work form part of the review covered in this article.

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