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Flavonoids and Isoflavonoids of *Millettia dura* and *Millettia ferruginea*: Phytochemical review and chemotaxonomic values

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ABSTRACT

The phytochemical information on *Millettia dura* Dunn, *M. ferruginea* (Hochst.) Baker and *M. ferruginea* subsp. *darassana* (Cufod.) J.B. Gillett was reviewed. All the three taxa elaborate mainly isoflavones (33 reported), occurring in the flowers, seeds/seed pods, stem bark and root bark. Out of the 33 isoflavones reported, some 19 (*ca*. 58%) contain prenyl at C-8 or its modification as 2,2-dimethylchromene ring at C-7/C-8, occurring in all the three taxa. Except for three isoflavones isolated from *M. ferruginea* subsp. *darassana*, all the isoflavones of these taxa are 5-deoxygenated. In these taxa, oxygenation at C-6 is a common feature, while isoflavones with C-8 oxygenation are rare, only three reported, and all of these from *M. dura*. There are 7 rotenoids reported from these taxa, and occur almost entirely in the seeds/seedpods of these plants. The major rotenoid with methylenedioxy group at C-2/C-3, millettone and its 12a-hydroxy derivative, millettosine, occur only in *M. dura*, this appears to distinguish *M. dura* from *M. ferruginea*.

1. Introduction

The genus *Millettia* Wight & Arn. belongs to the family of Leguminosae (Fabaceae) and subfamily Papilionoideae (Faboideae) (Ren et al., 2016; Deyou et al., 2015, 2017). This subfamily is characterised by the presence of papilinoid flowers, and has five hundred genera comprising of 14,000 species worldwide (Azani et al., 2017). The genus *Millettia* has about 260 species widely distributed over the tropical regions of Africa, Australia, Asia (Banzouzi et al., 2008; Dagne and Bekele, 1990; Chatsumpun et al., 2010; Havyarimana et al., 2012; Kamto et al., 2012; Zhi et al., 2013) and America (Kamto et al., 2012; Ren et al., 2016). Among these, 139 *Millettia* species are reported to be endemic to Africa (Banzouzi et al., 2008; Deyou et al., 2015). Plants of this genus are either trees (49%), climbers/lianas (38%) (Ngandeu et al., 2008) or shrubs (13%) (Deyou et al., 2017).

There are six *Millettia* species in Kenya namely; *M. dura, M. lasiantha, M. leucantha, M. oblata* subsp. *teitensis, M. tanaensis,* and *M. usaramensis* subsp. *usaramensis* (Beentje, 1994). Among these, *M. dura* is ecologically versatile and distributed naturally in moist forests in K1 and K4 regions of Kenya, extending to Tanzania and Uganda. It is often confused with the morphologically related taxon, *Millettia ferruginea* (Hochst.) Baker which is endemic to Ethiopia (Gillet et al., 1971; Hu et al., 2000; Dagne et al., 1991). The only difference between the two species is that, *M. dura* has narrower pods, longer and more spreading indumentum of its calyx and pedicel as well as absence of a cylindrical disc, observed in *M. ferruginea* (Gillet et al., 1971). *M. ferruginea* has an infraspecific taxon *M. ferruginea* subsp. *darassana* (The Plant List, 2013). The former is distributed in central and northern Ethiopia, while the latter is restricted to southern Ethiopia (Negash, 2010; Dagne et al., 1989). Both *M. dura* and *M. ferruginea* elaborate rotenoids with insecticidal activity (Yenesew et al., 2003a, b), and isoflavones with anticancer activity (Buyinza et al., 2019; Wang et al., 2020).

The chemotaxonomic value of flavonoids for some taxa in the family Leguminosae (Fabaceae) has been reported (Lima et al., 2017; Gomes et al., 1981). On the basis of the reported taxonomic confusion between *M. dura* and *M. ferruginea*, Dagne et al. (1991) compared the flavonoids and isoflavonoids isolated from these taxa and suggested that they were chemically distinct; *M. dura* elaborates C-8 oxygenated isoflavones, while *M. ferruginea* elaborates C-5 oxygenated isoflavones. Since this chemotaxonomic suggestion, several flavonoids and isoflavonoids have been described from these *Millettia* species. In view of this, the phytochemical information on *M. dura, M. ferruginea* and *M. ferruginea* subsp. *darassana* is reviewed, and also, the chemotaxonomic values of the flavonoids and isoflavonoids from these taxa are herein revisited. This review is based on phytochemical research done using organic solvent extracts of various plant parts (about 1 kg of each plant material) of *M.*

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Table 1
Distribution of chalcones, flavonoids and isoflavonoids in different parts of *Millettia dura* and *M. ferruginea*.

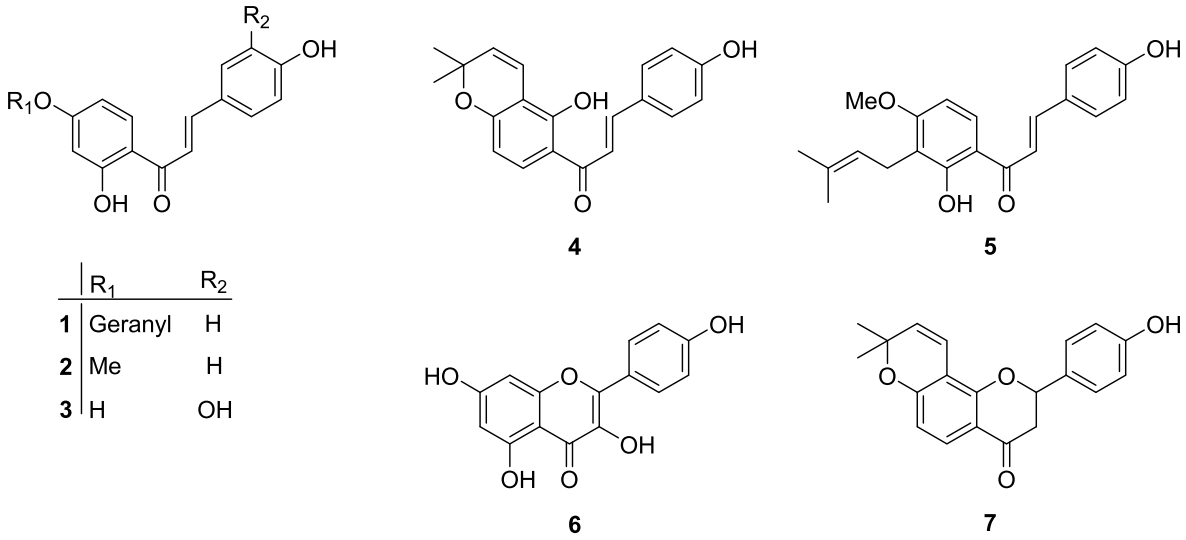
COMPOUND	Occurrence			
	Millettia dura	*M. ferruginea*		Other *Millettia* Species
		M. ferruginea subsp. *darassana*	*M. ferruginea* (Hochst.) Baker	
Chalcones				
4′-*O*-Geranylisoliquiritigenin (**1**)		RB (Dagne et al., 1990)		*M. usaramensis* subsp. *usaramensis* (RB) (Yenesew et al., 1998)
4,2′-Dihydroxy-4′-methoxychalcone (**2**)	FL (Buyinza et al., 2019)			
Butein (**3**)	RB (Marco et al., 2017)			
4-Hydroxylonchocarpin (**4**)	SB (Dagne et al., 1991)		SB (Dagne et al., 1989)	
4-Hydroxyderricin (**5**)	SB, RB (Dagne et al., 1991)			
Flavones				
Kampferol (**6**)	FL (Buyinza et al., 2019)			
Flavanone				
4′-Hydroxyisolonchocarpin (**7**)			SB (Dagne et al., 1989)	*M. pachycarpa* (SD) (Yanbei et al., 2019)
Isoflavones				
Barbigerone (**8**)	SB (Buyinza et al., 2019)	SD (Dagne and Bekele, 1990)	SD (Dagne and Bekele, 1990)	*M. usaramensis* subsp *usaramensis* (SB) (Yenesew et al., 1998), *M. dielsiana* Harms (ST) (Ye et al., 2014), *M. pachycarpa* (SD) (Tu et al., 2019)
Calopogoniumisoflavone A (**9**)	FL (Buyinza et al., 2019), SD, SB (Yenesew et al., 1996)	SD (Dagne and Bekele, 1990)	SD (Dagne and Bekele, 1990)	*M. oblata* subsp. *teitensis* (SB) (Derese et al., 2014), *M. dielsiana* (SB) (Ye et al., 2014)
Calopogoniumisoflavone B (**10**)	RB (Dagne et al., 1991; Marco et al., 2017)		SB (Dagne et al., 1989)	*M. griffoniana* (Yankep et al., 1997)
6-Demethydurallone (**11**)	SB (Yenesew et al., 1996)			
7,2′-Dimethoxy-4′, 5′-methylenedioxyisoflavone (**12**)	RB (Dagne et al., 1991; Marco et al., 2017)			
7,3′-Dimethoxy-4′,5′-methylenedioxyisoflavone (**13**)	SB (Derese et al., 2003)			
7-Hydroxy-8,3′,4′-trimethoxylisoflavone (**14**)	RB (Marco et al., 2017)			*M. usaramensis* subsp *usaramensis* (RB) (Deyou et al., 2015)
Durallone (**15**)	FL (Buyinza et al., 2019); SD, SB (Yenesew et al., 1996)			*M. oblata* subsp. *teitensis* (ST) (Derese et al., 2014) and *M. dielsiana* (ST) (Ye et al., 2014).
Durlettone (**16**)	SD (Ollis et al., 1967; Dagne et al., 1991)			
Durmillone (**17**)	FL (Buyinza et al., 2019); SB (Yenesew et al., 1996); RB (Marco et al., 2017); SD (Ollis et al., 1967)	SP (Dagne et al., 1989); SD (Dagne and Bekele, 1990)	SD (Dagne and Bekele, 1990)	*M. grifoniana* (RB) (Yankep et al., 1997),
6,7-Dimethoxy-3′,4′-methylenedioxy-8-(3,3-dimethylallyl) isoflavone (**18**)			SD (Deyou and Jang, 2018)	
Ferrugone (**19**)	SB (Buyinza et al., 2019); SD (Ollis et al., 1967); SP (Yenesew et al., 1997)	SB (Dagne et al., 1989); SD (Dagne and Bekele, 1990)	SB (Dagne et al., 1989); SD (Dagne and Bekele, 1990)	
Formononetin (**20**)	FL (Buyinza et al., 2019); SP (Yenesew et al., 1997)			
7-*O*-Geranylformononetin (**21**)		RB (Dagne et al., 1990)		
7-Hydroxy-5,6-dimethoxy-3′,4′-methylenedioxisoflavone (**22**)		SB (Dagne et al., 1989)		
Ichthynone (**23**)	FL (Buyinza et al., 2019); SB (Ollis et al., 1967)	SB (Dagne et al., 1989)		*M. caerulea* (FT) (Ren et al., 2016), *M. pachyloba* (GR) (Mai et al., 2010), *M. dielsiana* (ST) (Ye et al., 2014)
Isoerythrin A, 4′-(3-methylbut-2-enyl) ether (**24**)	SB (Yenesew et al., 1996); RB (Derese et al., 2003; Marco et al., 2017)			
Isojamaicin (**25**)	SB (Derese et al., 2003)		SB (Dagne et al., 1989)	*M. usaramensis* subsp. *usaramensis* (SB) (Derese et al., 2003; Yenesew et al., 1998)
Jamaicin (**26**)	FL, SB (Buyinza et al., 2019); SP (Yenesew et al., 1997)	SB (Dagne et al., 1989); RB (Dagne and Bekele, 1990)	SB (Dagne et al., 1989)	*M. usaramensis* subsp. *usaramensis* (SB) (Yenesew et al., 1998), *M. grifoniana* (RB), *M. pachyloba* (GR) (Mai et al., 2010).
Maximaisoflavone B (**27**)	SB (Dagne et al., 1991); RB (Marco et al., 2017)			*M. oblata* subsp. *teitensis* (LV) (Deyou et al., 2017)
Maximaisoflavone D (**28**)	SB (Yenesew et al., 1996)			
Maximaisoflavone G (**29**)	SB (Buyinza et al., 2019)			*M. oblata* subsp. *teitensis* (LV) (Deyou et al., 2017)

(*continued on next page*)

Table 1 (*continued*)

COMPOUND	Occurrence			
	Millettia dura	*M. ferruginea*		Other *Millettia* Species
		M. ferruginea subsp. *darassana*	*M. ferruginea* (Hochst.) Baker	
Maximaisoflavone H (**30**)	SB & RB (Dagne et al., 1991; Yenesew et al., 1996)			*M. oblata* (RB) (Deyou et al., 2015)
Maximaisoflavone J (**31**)	FL, SB (Buyinza et al., 2019)			*M. oblata* subsp. *teitensis* (ST, LV) (Deyou et al., 2017)
5-Methoxydurmillone (**32**)		SB (Dagne et al., 1989), RB (Dagne and Bekele, 1990)	SB (Dagne et al., 1989)	
6-Methoxylcalopogoniumisoflavone A (**33**)	FL (Buyinza et al., 2019); SD (Yenesew et al., 1997)			*M. dielsiana* (ST) (Ye et al., 2014), *M. oblata* subsp. *teitensis* (ST) (Derese et al., 2014)
Milldurone (**34**)	SD (Ollis et al., 1967)			*M. oblata* subsp. *teitensis* (LV) (Deyou et al., 2017)
Nordurlettone (**35**)	RB (Derese et al., 2003)	RB (Dagne et al., 1990)		
Pre-5-methoxydurmillone (**36**)		RB (Dagne and Bekele, 1990)		
Prebarbigerone (**37**)			SD (Dagne and Bekele, 1990)	
Predurallone (**38**)	SP (Yenesew et al., 1996)			
Predurmillone (**39**)		SD (Dagne and Bekele, 1990)		
Preferrugone (**40**)		SD (Dagne and Bekele, 1990)		
Rotenoids				
Deguelin (**41**)	SD (Ollis et al., 1967); SP (Buyinza et al., 2019)		SD (Dagne et al., 1991)	*M. pachycarpa* (SD) (Tu et al., 2019)
6a,12a-Dehydrodeguelin (**42**)	SD (Ollis et al., 1967)			*M. oblata* subsp. *teitensis* (LV) (Deyou et al., 2017)
12a-Hydroxyrotenone (**43**)		SD (Dagne and Bekele, 1990)		*M. pachycarpa* (SD) (Tu et al., 2019)
Millettone (**44**)	SD (Ollis et al., 1967); SP (Yenesew et al., 1997)			
Millettosin (**45**)	SD (Ollis et al., 1967)			*M. usaramensis* subsp *usaramensis* (RB, SB) (Deyou et al., 2015; Yenesew et al., 1998)
Rotenone (**46**)	SD (Ollis et al., 1967)		SD (Dagne and Bekele, 1990)	*M. pachycarpa* (SD), (Ashok et al., 1982)
Tephrosin (**47**)	SD (Ollis et al., 1967); SP (Yenesew et al., 1997; Buyinza et al., 2019)	SD (Dagne and Bekele, 1990)		*M. oblata* subsp. *teitensis* (RB, LV) (Deyou et al., 2015, 2017), *M. usaramensis* subsp. *usaramensis* (SD) (Yenesew et al., 1998), *M. usaramensis* subsp. *usaramensis* (RB) (Deyou et al., 2015), *M. pachycarpa* (SD) (Tu et al., 2019)
Pterocarpanoids				
Flemichapparin B (**48**)	SB (Dagne et al., 1989)	SB (Dagne et al., 1989)		
3-*O*-Prenylmaackiain (**49**)	RB Marco et al. (2017)			

Key: LV Leaves, FL Flowers, SP Seed pods, SD seeds, FT Fruits, GR Grains, SB Stem bark, ST Stems, RB Root bark.



	R_1	R_2
1	Geranyl	H
2	Me	H
3	H	OH

Fig. 1. Structures of chalcones, flavonols and flavanones from *M. dura* and *M. ferruginea*.

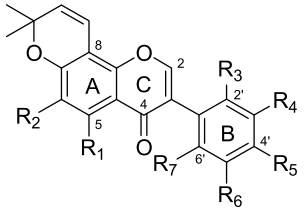
dura (Buyinza et al., 2019; Derese et al., 2003; Marco et al., 2017; Ollis et al., 1967; Yenesew et al., 1996, 1997), *Millettia ferruginea* (Deyou and Jang, 2018), and *M. ferruginea* subsp. *darassana* (Dagne et al., 1989; Dagne and Bekele, 1990; Dagne et al., 1990).

2. The flavonoids and isoflavonoids of *Millettia dura* and *M. ferruginea*

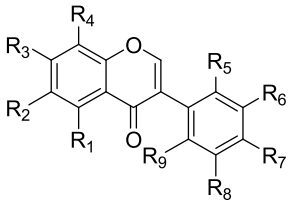
The compounds isolated from *M. dura*, *M. ferruginea* and *M. ferruginea* subsp. *darassana* are presented in Table 1. From these taxa, chalcones, a flavanone and a flavonol (Fig. 1), isoflavones (Fig. 2), rotenoids and pterocarpanoids (Fig. 3) have been reported. The presence of these compounds in other *Millettia* species has also been included in Table 1.

2.1. Chalcones, Flavonols and Flavanones

From the three taxa, a total of five chalcones (**1–5**) have been reported (Table 1; Fig. 1). Whereas compounds **2** and **3** isolated from *M. dura* are simple chalcones which appear to be precursors to several flavonoids of these taxa, compounds **4** and **5** are *C*-prenylated. Compound **1** is geranylated and has been reported from *M. ferruginea* subsp. *darassana* (Dagne et al., 1989), its occurrence in *M. usaramensis* subsp. *usaramensis* (Yenesew et al., 1998) has also been reported. Four of the five chalcones have been reported from *M. dura*. A flavonol (**6**) isolated from the flowers of *M. dura* (Buyinza et al., 2019) and a flavanone (**7**) from the stem bark of *M. ferruginea* (Dagne et al., 1989) represent simple flavonoids which occur widely in different genera of the family Leguminosae, and have little chemotaxonomic value.



	R_1	R_2	R_3	R_4	R_5	R_6	R_7
8	H	H	OMe	H	OMe	OMe	H
9	H	H	H	H	OMe	H	H
10	H	H	H		OCH_2O	H	H
15	H	OMe	H	OMe	OMe	H	H
17	H	OMe	H		OCH_2O	H	H
19	H	H	OMe		OCH_2O	OMe	H
23	H	OMe	H		OCH_2O	H	OMe
24	H	H	H	H	O-Prenyl	H	H
25	H	H	H		OCH_2O	OMe	H
26	H	H	H		OCH_2O	H	OMe
32	OMe	OMe	H		OCH_2O	H	H
33	H	OMe	H	H	OMe	H	H



	R_1	R_2	R_3	R_4	R_5	R_6	R_7	R_8	R_9
11	H	OH	OMe	Prenyl	H	OMe	OMe	H	H
12	H	H	OMe	H	H		OCH_2O	OMe	H
13	H	H	OMe	H	H		OCH_2O	H	OMe
14	H	H	OH	OMe	H	H	OMe	OMe	H
16	H	H	OMe	H	H	H	O-Prenyl	H	H
18	H	OMe	OMe	Prenyl	H		OCH_2O	H	H
20	H	H	OH	H	H	H	OMe	H	H
21	H	H	O-Geranyl	H	H	H	OMe	H	H
22	OMe	OMe	OH	H	H		OCH_2O	H	H
27	H	H	O-Prenyl	H	H		OCH_2O	H	H
28	H	H	OCH_2O		H	OMe	OMe	H	H
29	H	H	OH	H	H		OCH_2O	OMe	H
30	H	H	OCH_2O		H	H	OMe	H	H
31	H	H	O-Prenyl	H	H	H	OMe	H	H
34	H	OMe	OMe	H	H		OCH_2O	OMe	H
35	H	H	OH	H	H	H	O-Prenyl	H	H
36	OMe	OMe	OH	Prenyl	H		OCH_2O	H	H
37	H	H	OMe	Prenyl	OMe	H	OMe	OMe	H
38	H	OMe	OH	Prenyl	H	OMe	OMe	H	H
39	H	OMe	OH	Prenyl	H		OCH_2O	H	H
40	H	H	OH	Prenyl	OMe		OCH_2O	OMe	H

Fig. 2. Structures of isoflavones from *M. dura* and *M. ferruginea*.

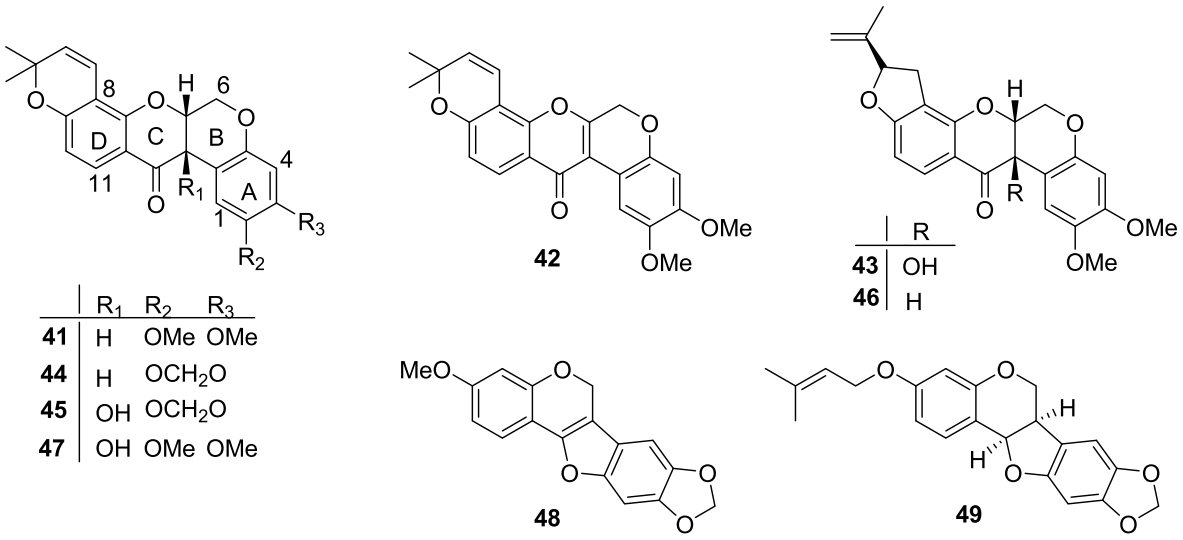


Fig. 3. Structures of rotenoids and pterocarpanoids from *M. dura* and *M. ferruginea*.

2.2. Isoflavones

A total of 33 isoflavones (Fig. 2) have so far been reported from *M. dura, M. ferruginea*; and *M. ferruginea* subsp. *darassana;* among these 19 contain a *C*-prenyl group at C-8, or its modification into a 2,2-dimthylchromene ring involving the hydroxy group at C-7. Such compounds occur in all the three taxa (Table 1). *C*-prenylation has not been observed at any other position other than C-8. There are 5 examples of *O*-prenylated isoflavones (**16**, **24**, **27**, **31** and **35**), at either C-7 or C-4′ occurring in *M. dura,* and among these, only compound **35** was reported from *M. ferruginea* subsp. *darassana*. There is only one example of *O*-geranylated isoflavones (compound **21**), reported from *M. ferruginea* subsp. *darassana* (Table 1). The rest of the 14 isoflavones are simpler isoflavones substituted with methoxy and/or methylenedioxy groups. There are 9 isoflavones (Table 1) with a free hydroxy group. Except for 6-demethyldurallone (**11**) where the free hydroxy group is at C-6, the free hydroxy group in the other isoflavones of these taxa is at C-7. These isoflavones, upon methylation or cyclization involving the adjacent prenyl group, produce the corresponding alkylated isoflavones which co-occur in these plants.

Except for three isoflavones (**22**, **32** and **36**) occurring only in *M. ferruginea* subsp. *darassana*, all the other isoflavones reported are 5-deoxy derivatives. This indicates that they are likely to have been derived from the chalcone isoliquiritigenin, through the flavanone liquiritigenin mediated by the enzyme CHI (Andrej et al., 2004). In ring A, in addition to the biogenetically expected oxygenation at C-7, oxygenation has been observed at C-6 in 12 of these isoflavones (Table 1, **11**, **15**, **17**, **18**, **22**, **23**, **32–34**, **36**, **38** and **39**). Out of these, 7 compounds (**11**, **15**, **17**, **23**, **33**, **34** and **38**) were reported from *M. dura*, 6 compounds (**17**, **22**, **23**, **32**, **36** and **39**) from *M. ferruginea* subsp. *darassana*, and 3 compounds (**17**, **18** and **32**) from *M. ferruginea.* Among the C-6 oxygenated isoflavones, only compound **17** is shared among these three taxa. On the other hand, oxygenation at C-8 is rare but has been observed in three isoflavones (**14**, **28** and **30**), all isolated from *M. dura*.

A methylenedioxy group in ring A has been reported for compounds **28** and **30** isolated from *M. dura.* However, this is a more common feature in ring B as found in 16 isoflavones (**10**, **12**, **13**, **17–19**, **22**, **23**, **25–27**, **29**, **30**, **32**, **36**, **39** and **40**). In ring B, in addition to the biogenetically expected oxygenation at C-4′, oxygenation has been observed at C-2′ or C-6′ in 7 isoflavones (**8**, **13**, **19**, **23**, **26**, **37** and **40**). The more preferred additional oxygenation in ring B is at C-3′ or C-5′, with 24 isoflavones (Table 1) oxygenated at one of these two positions. Among these, 6 compounds (**12**, **19**, **25**, **29**, **34** and **40**) are oxygenated at both C-3′ and C-5′, a feature more common in *M. dura*, having 5 compounds (**12**, **19**, **25**, **29** and **34**) than in *M. ferruginea* subsp. *darassana* (one isoflavone, **19**) and *M. ferruginea* (two isoflavones, **19** and **25**).

2.3. Rotenoids

A total of seven rotenoids have been reported from *M. dura* and the two taxa of *M. ferruginea,* all of which having a pyran (**41**, **42**, **44**, **45** and **47**) or furan (**43** and **46)** rings attached to ring D, at C-8/C-9. Two of these (**44**, and **45**) have a methylenedioxy group between C-2 and C-3 in ring A, while the rest have two methoxy groups at these positions. All the reported rotenoids are C-11 deoxygenated and only **42** is a 6a,12a-dehydrorotenoid. It is only tephrosin (**47**) which has been reported across the three taxa, while **41** and **46** are shared between *M. dura* and *M. ferruginea* yet compound **43** is shared between *M. dura* and *M. ferruginea* subsp. *darassana*. The occurrence of compounds **44** and **45** has only been reported from *M. dura*, and appears to distinguish this taxon from *M. ferruginea*. The B/C ring junction in all these rotenoids and 12a-hydroxyrotenoids is *cis*-oriented having the same absolute configuration with (6a*S*,12a*S*) designation for the rotenoids (**41**, **44**, and **46**), and (6a*R*,12a*R*) designation for the 12a-hydroxyrotenoids (**43**, **45** and **47**) as determined by ORD (Ollis et al., 1967). Of the two pterocarpans reported, flemichapparin B (**48**) is shared between *M. dura* and *M. ferruginea* subsp. *darassana,* while 3-*O*-prenylmaackianin (**49**) has only been reported from *M. dura*.

3. Chemotaxonomic significance of flavonoids and isoflavonoids

Whereas, the occurrence of several isoflavones and rotenoids in *M. dura* and *M. ferruginea* supports the morphological similarities of these taxa, there appears to be some differences which may be useful to distinguish these taxa. C-6 oxygenated isoflavones are common in all the three taxa; on the other hand, C-8 oxygenation (compounds **14**, **28** and **30**) has only been observed in *M. dura.* The *O*-prenylated isoflavone isoerythrine A 4′-(3-methylbut-2-enyl) ether (**24**), the isoflavones 6-demethyldurallone (**11**), durallone (**15**), durlettone (**16**) have only been reported from *M. dura*. The rotenoids millettone (**44**) and millettosine (**45**) with methylenedioxy group at C-2/C-3, appear to delineate *M. dura* from the two taxa of *M. ferruginea.* The C-5 oxygenated isoflavones; 7-hydroxy-5,6-dimethoxy-3′,4′-methylenedioxyisoflavone (**22**), 5-methoxydurmillone (**32**) and pre-5-methoxydurmillone (**36**) from the two taxa of *M. ferruginea,* have not been reported from *M. dura*. The geranylated chalcone 4′-*O*-geranylisoliquiritigenin (**1**) and

the isoflavone 4′-*O*-geranylformononetin (**21**) have been isolated from the root bark of *M. ferruginea,* subsp. *darassana.* These compounds have not been reported from the roots of *M. dura*, however, the chemotaxonomic values of these compounds could not be fully appreciated since phytochemical information is not available on the roots *M. ferruginea.*

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.bse.2020.104053.

References

Andrej, J., Juraj, F., Ivana, P., Tibor, M., 2004. Approaches to flavonoid production in plant tissue cultures-Review. Biol Bratisl 59, 697–710.

Ashok, K.S., Itankar, P.S., Jogendra, N.B., Serengolam, V.G., Werner, H., 1982. Rotenoids from roots of *Millettia pachycarpa*. Phytochemistry 21, 949–951.

Azani, N., Babineau, M., Bailey, C.D., Banks, H., Barbosa, A.R., Pinto, R.B., Boatwright, J.S., Borges, L.M., Brown, G.K., Bruneau, A., Candido, E., Cardoso, D., Chung, K.-F., Clark, R.P., Conceição, A. de S., Crisp, M., Cubas, P., Delgado-Salinas, A., Dexter, K.G., Zimmerman, E., 2017. A new subfamily classification of the Leguminosae based on a taxonomically comprehensive phylogeny: the Legume Phylogeny Working Group (LPWG). Taxon 66, 44–77. https://doi.org/10.12705/661.3.

Banzouzi, J.T., Prost, A., Rajemiarimiraho, M., Congo, P., 2008. Traditional uses of the african *Millettia* species (fabaceae). Int. J. Bot. 4, 406–420.

Beentje, H.J., 1994. Kenya Trees, Shrubs and Lians. The National Museums of Kenya, Nairobi.

Buyinza, D., Yang, L.J., Derese, S., Ndakala, A., Coghi, P., Heydenreich, M., Wong, V.K.W., Moller, H., Abiy, Y., 2019. Cytotoxicity of isoflavones from *Millettia dura*. Nat. Prod. Res. https://doi.org/10.1080/14786419.2019.1660335.

Chatsumpun, M., Sritularak, B., Likhitwitayawuid, K., 2010. Phenolic compounds from stem wood of *Millettia leucantha*. Chem. Nat. Compd. 46, 634–635.

Dagne, E., Bekele, A., 1990. *C*-prenylated isoflavones from *Millettia ferruginea*. Phytochemistry 29, 2679–2682.

Dagne, E., Bekele, A., Waterman, P.G., 1989. The Flavonoids of *Millettia ferruginea* ssp. *ferruginea* and ssp. *darassana* in Ethiopia. Phytochemistry 28, 1897–1900.

Dagne, E., Bekele, A., Noguchi, H., Shibuya, M., Sankawa, U., 1990. *O*-Geranylated and *O*-prenylated flavonoids from *Millettia ferruginea*. Phytochemistry 29, 2671–2673.

Dagne, E., Wendimagegn, M., Amha, B., 1991. Flavanoids of *Millettia dura*. Bull. Chem. Soc. Ethiop. 5, 81–86.

Derese, S., Yenesew, A., Midiwo, J.O., Heydenreich, M., Peter, M.G., 2003. A new isoflavone from stem bark of *Millettia dura*. Bull. Chem. Soc. Ethiop. 17, 113–115.

Derese, S., Barasa, L., Akala, H.M., Yusuf, A.O., Kamau, E., Heydenreich, M., Yenesew, A., 2014. 4′-Prenyloxyderrone from the stem bark of *Millettia oblata* ssp. *teitensis* and the antiplasmodial activities of isoflavones from some *Millettia* species. Phytochem Lett 8, 69–72. https://doi.org/10.1016/j.phytol.2014.02.001.

Deyou, T., Jang, Y.P., 2018. A new prenylated isoflavone from the seeds of *Millettia ferruginea* ssp. *ferruginea*. S Afr J Bot. 117, 155–157.

Deyou, T., Gumula, I., Pang, F., Gruhonjic, A., Mumo, M., Holleran, J., Duffy, S., Fitzpatrick, P.A., Heydenreich, M., Landberg, G., Derese, S., Avery, V., Rissanen, K., Erdélyi, M., Yenesew, A., 2015. Rotenoids, flavonoids, and chalcones from the root bark of *Millettia usaramensis*. J. Nat. Prod. 78, 2932–2939. https://doi.org/10.1021/acs.jnatprod.5b00581.

Deyou, T., Marco, M., Heydenreich, M., Pan, F., Gruhonjic, A., Fitzpatrick, P.A., Koch, A., Derese, S., Pelletier, J., Rissanen, K., Yenesew, A., Erdélyi, M., 2017. Isoflavones and rotenoids from the Leaves of *Millettia oblata* ssp. *teitensis*. J. Nat. Prod. 80, 2060–2066. https://doi.org/10.1021/acs.jnatprod.7b00255.

Gillet, J.B., Polhill, M.R., Verdcourt, B., 1971. Flora of Tropical East Africa-*Leguminosae*. Whitefrias Press Ltd, Great Britain, pp. 123–144.

Gomes, C.M.R., Gottlieb, O.R., Marini, B.G.B., Delle, M.F., Polhill, R.M., 1981. Systematic significance of flavonoids in *Derris* and *Lonchocarpus*. Biochem. Systemat. Ecol. 9, 129–147.

Havyarimana, L., Ndendoung, S.T., de Dieu Tamokou, J., de Théodore Atchadé, A., Tanyi, J.M., 2012. Chemical constituents of *Millettia barteri* and their antimicrobial and antioxidant activities. Pharm. Biol. 50, 141–146. https://doi.org/10.3109/13880209.2011.579618.

Hu, J.-M., Lavin, M., Wojciechowski, M.F., Sanderson, M.J., 2000. Phylogenetic systematics of the tribe Millettieae (Leguminosae) based on chloroplast *trn K/mat K* sequences and its implications for evolutionary patterns in Papilionoideae. Am. J. Bot. 87, 418–430. https://doi.org/10.2307/2656638.

Kamto, E.L.D., Atchadé, A. de T., Marston, A., Pegnyemb, D.E., van der Westhuizen, J.H., 2012. Chemical constituents from bark of *Millettia mannii* baker (Papilionoideae – Leguminosae). Biochem. Systemat. Ecol. 45, 98–101. https://doi.org/10.1016/j.bse.2012.07.006.

Lima, N.M., Santos, V.N.C., Alessandra de Paula Carli, A.de-P., Christiane, P., Soares, C.P., 2017. Genus *deguelia*: chemistry, chemotaxonomy, ethnopharmacology and pharmacological characteristics – a review. Pharm. Chem. J. 4, 13–26.

Mai, H.D.T., Nguyen, T.T.O., Cuong, V., Pham, M.L., Guéritte, F., Tran, D.T., 2010. Cytotoxic prenylated isoflavone and bipterocarpan from *Millettia*. Planta Med. 76, 1739–1742.

Marco, M., Deyou, T., Gruhonjic, A., Holleran, J., Duffy, S., Heydenreich, M., Firtzpatrick, P.A., Landberg, G., Koch, A., Derese, S., Pelletier, J., Avery, V.M., Erdélyi, M., Yenesew, A., 2017. Pterocarpans and isoflavones from the root bark of *Millettia micans* and of *Millettia dura*. Phytochem Lett 21, 216–220. https://doi.org/10.1016/j.phytol.2017.07.012.

Negash, L., 2010. A Selection of Ethiopia's Indigenous Trees: Biology, Uses, and Propagation Techniques. Addis Ababa Univ. Press.

Ngandeu, F., Bezabih, M., Ngamga, D., Tchinda, A.T., Ngadjui, B.T., Abegaz, B.M., Dufat, H., Tillequin, F., 2008. Rotenoid derivatives and other constituents of the twigs of *Millettia duchesnei*. Phytochemistry 69, 258–263. https://doi.org/10.1016/j.phytochem.2007.05.038.

Ollis, W.D., Rhodes, C.A., Sutherland, I.O., 1967. The extractives of *Millettia dura* (Dunn): the constitutions of durlettone, durmillone, milldurone, millettone and millettosin. Tetrahedron 23, 4741–4760.

Ren, Y., Benatrehina, P.A., Muñoz Acuña, U., Yuan, C., Chai, H.B., Ninh, T.N., Carcache De Blanco, E.J., Soejarto, D.D., Kinghorn, A.D., 2016. Isolation of bioactive rotenoids and isoflavonoids from the Fruits of *Millettia caerulea*. Planta Med. 82, 1096–1104. https://doi.org/10.1055/s-0042-108059.

The Plant List, 2013. A working list of all plant species. www.worldfloraonline.org (accessed 09th April, 2020).

Tu, Y., Xiao, T., Gong, G., Bian, Y., Li, Y., 2019. A new isoflavone with anti-inflammatory effect from the seeds of *Millettia pachycarpa*. Nat. Prod. Res. 1–7. https://doi.org/10.1080/14786419.2018.1547294.

Wang, Y.-Y., Jun Hyeok Kwak, J.H., Lee, K.-T., Deyou, T., Jang, Y.P., Choi, J.-H., 2020. Isoflavones isolated from the seeds of *Millettia ferruginea* induced apoptotic cell death in human ovarian cancer cells. Molecules 25, 207. https://doi.org/10.3390/molecules25010207.

Yanbei, T., Wu, C., Kang, Y., Li, Q., Zhu, C., Li, Y., 2019. Bioactivity-guided identification of flavonoids with cholinesterase and β-amyloid peptide aggregation inhibitory effects from the seeds of *Millettia pachycarpa*. Bioorg. Med. Chem. Lett 29, 1194–1198. https://doi.org/10.1016/j.bmcl.2019.03.024.

Yankep, E., Fomum, Z.T., Dagne, E., 1997. An *O*-geranylated isoflavone from *Millettia griffoniana*. Phytochemistry 46, 591–593.

Ye, H., Wu, W., Liu, Z., Xie, C., Tang, M., Li, S., Yang, J., Tang, H., Chen, K., Long, C., Peng, A., Wei, Y., Chen, L., 2014. Bioactivity-guided isolation of anti-inflammation flavonoids from the stems of *Millettia dielsiana* Harms. Fitoterapia 95, 154–159. https://doi.org/10.1016/j.fitote.2014.03.008.

Yenesew, A., Midiwo, J.O., Waterman, P.G., 1996. Four isoflavones from seed pods of *Millettia dura*. Phytochemistry 41, 951–955. https://doi.org/10.1016/0031-9422(95)00662-1.

Yenesew, A., Midiwo, J.O., Waterman, P.G., 1997. 6-Methoxycalpogonium isoflavone A: a new isoflavone from the seed pods of *Millettia dura*. J. Nat. Prod. 60, 806–807. https://doi.org/10.1021/np9605955.

Yenesew, A., Midiwo, J.O., Waterman, P.G., 1998. Rotenoids, isoflavones and chalcones from the stem bark of *Millettia usaramensis* subspecies *usaramensis*. Phytochemistry 47, 295–300.

Yenesew, A., Derese, S., Midiwo, J.O., Heydenreich, M., Peter, M.G., 2003a. Effect of rotenoids *from Millettia dura* on larvae of *Aedes aegypti*. Pest Manag. Sci. 59, 1157–1161.

Yenesew, A., Derese, S., Midiwo, J.O., Oketch-Rabah, H.A., Lisgarten, J., Palmer, R., Heydenreich, M., Peter, M.G., Akala, H., Wangui, J., Liyala, P., Waters, N.C., 2003b. Anti-plasmodial activities and X-ray crystal structures of rotenoids from *Millettia usaramensis* subspecies *usaramensis*. Phytochemistry 64, 773–779. https://doi.org/10.1016/S0031-9422(03)00373-X.

Zhi, Na, Song, Qishi, Hu, Huabin, 2013. Flavonoids from twigs of *Millettia leptobotrya Dunn*. Record Nat. Prod. 7, 307–312.