Pterocarpans and Isoflavones from the Root Bark of *Millettia micans* and of *Millettia dura*

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Abstract: From the CH_2Cl_2/CH_3OH (1:1) extract of the root bark of *Millettia micans*, a new pterocarpan, (6a*R*,11a*R*)-7,8,9-trimethoxy-3-hydroxypterocarpan (**1**), named micanspterocarpan, was isolated. Similar investigation of the CH_2Cl_2/CH_3OH (1:1) extract of the root bark of *Millettia dura* gave a further new pterocarpan, 3-*O*-prenylmaackiain (**2**) along with six known isoflavones (**3-8**) and a chalcone (**9**). All purified compounds were identified by NMR and MS, and the absolute configuration of **1** was established by quantum chemical CD calculation. The isolated constituents, calopogonium isoflavone B (**3**) and isoerythrin A-4'-(3-methylbut-2-enyl) ether (**4**) showed marginal activities against the 3D7 and the Dd2 strains of *Plasmodium falciparum* (70-90% inhibition at 40 μM). Maximaisoflavone B (**5)** and 7,2'-dimethoxy-4',5'-methylenedioxyisoflavone (**7**) were weakly cytotoxic (IC_{50} 153.5 and 174.1 μM, respectively) against the MDB-MB-231 human breast cancer cell line. None of the tested compounds showed toxicity against the HEK-293 human embryonic kidney cell line at 40 μM.

Dedicated to the late Professor Joseph Magadula

Keywords: *Millettia micans*; *Millettia dura*; Micanspterocarpan; 3-*O*-Prenylmaackiain; Pterocarpan; Isoflavone; Cytotoxicity; *Plasmodium falciparum*.

INTRODUCTION

The genus *Millettia* (family Leguminosae, subfamily Papilionoideae) with approximately 260 species is widespread in Africa (139 species) and in Asia (121 species) [1]. Out of the East African countries, the highest number of *Millettia* species, 25, are endemic to Tanzania, followed by 6 species native to Kenya [1]. The genus is a rich source of secondary metabolites such as chalcones, iso flavones, rotenoids [2,3], isoflavans [4], flavanones, coumarins [5] and pterocarpans [6]. Some of these metabolites inhibit nitric oxide formation or possess larvicidal, pesticidal, cytotoxic, antiinflammatory, antimicrobial and cancer chemopreventive activities [1].

Millettia dura (Dunn), growing in both Tanzania and Kenya, is used as food for livestock, as a source of firewood and charcoal, and as timber for construction since it is tough and resistant to termites [7]. Traditionally, in various parts of Africa, it is used to treat hemias, diarrheas, menstrual irregularities and for healing wounds [1]. Its seeds, seed pods, stem and root bark have been reported to contain rotenoids and isoflavones [8-12]. In contrast, *Millettia micans* (Taub), a vulnerable small tree endemic to Tanzania, has no documented traditional uses and has not yet been phytochemically explored.

Here, we report the isolation and characterization of two new pterocarpans, named micanspterocarpan (**1**) and 3-*O*-prenylmaackiain (**2**), from the root bark of *Millettia micans* and *Millettia dura*, respectively. From the roots of *Millettia dura*, seven additional known compounds (**3**-**9**) were also identified. The antiplasmodial and cytotoxicity profiles of

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a selection of the isolated compounds are also presented.

RESULTS AND DISCUSSION

Column chromatographic separation of the CH_2Cl_2/CH_3OH (1:1) extract of the root bark of *Millettia micans* resulted in the isolation of a new pterocarpan (**1**, Figure **1**). HRMS (EI) indicated the molecular formula $C_{18}H_{18}O_6$ (*m/z* obs, 330.1115 $[M]^+$, calcd 330.1103), whereas the UV absorption maxima 268 and 281 nm, and ^1H NMR (H-6*eq*, H-6*ax,* H-6a, H-11a) and ^{13}C NMR (C-6a, C-6, C-11a) spectral data (Table **1**) were consistent with a pterocarpan skeleton [13,14]. Three methoxy substituents, OCH_3-7, OCH_3-8 and OCH_3-9, three protons in an ABX spin system (H-1, H-2, H-4), and a singlet aromatic proton, H-10, suggested **1** to be a tetrasubstituted pterocarpan. The HMBC correlation of the methine proton at δ_H 5.43 (H-11a) with δ_c 132.4 (C-1) allowed the assignment of the ABX spin system to ring A. The aromatic singlet at δ_H 6.21 was assigned to H-10 of ring D, which is otherwise fully substituted. HMBC correlation of this proton (δ_H 6.21) to C-6b (δ_c 110.0), C-8 (δ_c 135.7), C-9 (δ_c 155.0) and C-10a (δ_c 156.1), and the absence of HMBC correlation to C-6a (δ_c 39.3) is consistent to it being assigned to H-10, instead of the alternative H-7. The high chemical shifts of C-7, C-8 and C-9 of ring D reveal these to be oxygenated (Table **1**). The deshielding of two of the methoxy groups (δ_c 61.0 and 61.1) indicated diortho substitution [15], and they were hence placed at C-7 and C-8. The connection of the third methoxy group (δ_H 3.77, δ_c 56.3) to C-9 (δ_c 155.0) was indicated by their HMBC correlation, and by the NOE correlation of OCH_3-9 and H-10 (δ_H 6.21). The $^3J_{H\text{-}6a,H\text{-}11a}$=7.0 Hz is typical of the energetically more favorable *cis* B/C ring junction [16]. This relative configuration was further corroborated by the strong NOE observed between H-6a and H-11a that is in excellent agreement with the calculated (B3LYP/6-311G**) 2.4 Å distance between these protons in the lowest energy geometry of the *cis*-fused configurational isomer (Figure **2**).

A large and negative optical rotation ($[\alpha]_D$ -134.3°) and a negative Cotton effect at 232.6 nm (Figure **3**) in its CD spectrum were consistent with the 6a*R*,11a*R* absolute configuration of the B/C ring junction [16,17], which was confirmed by theoretical CD calculations. It was further noted that a different orientation of the methoxy and the hydroxy groups is predicted to lead to asymmetric behavior, concerning H-6a and H-11a, of the calculated CD spectra of 6a*R,*11a*R* (Figure **2a**) and the 6a*S,* 11a*S* (Figure **2b**), the latter being 0.36 kcal/mole higher in energy. The orientation of these func-

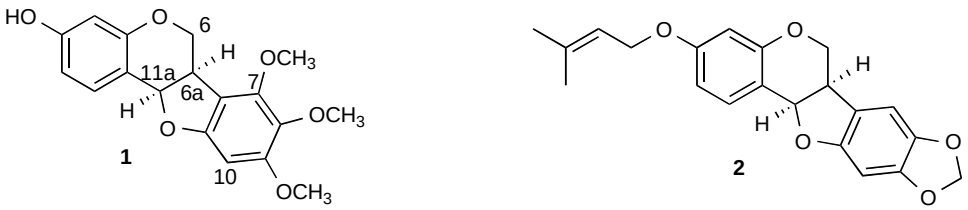

Figure 1: Micanspterocarpan (**1**) and 3-*O*-prenylmaackiain (**2**), the pterocarpans isolated from *Millettia micans* and *Millettia dura*, respectively.

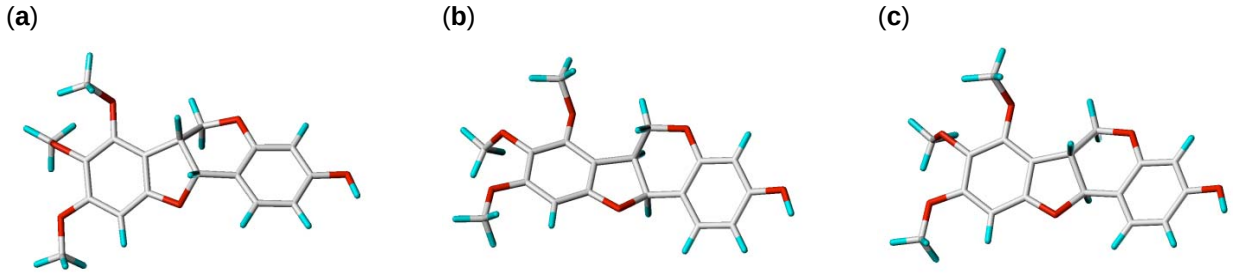

Figure 2: The calculated global energy minimum geometries of (**a**) the *cis*-fused 6a*R*,11aR-**1**, (**b**) the *cis*-fused 6aS,11aS-**1** (**c**), and of the *trans*-fused 6aR,11aS-**1**.

Table 1: ^{1}H and ^{13}C NMR Data for Micanspterocarpan (1) and for 3-*O*-Prenylmaackiain (2), Acquired in CD_2Cl_2 and $CDCl_3$, Respectively

	Micanspterocarpan (1)			3-*O*-Prenylmaackiain (2)		
	δ_H (*J* in Hz)	δ_c	HMBC	δ_H (*J* in Hz)	δ_c	HMBC
1	7.32 (*d*, 8.4)	132.4	3,11a, 4a	7.39 (*d*, 8.8)	131.7	3, 4a, 11a
2	6.52 (*dd*, 8.4, 2.5)	109.7	4, 11b	6.64 (*dd*, 2.4, 8.8)	109.8	4, 11b
3		157.4			160.3	
4	6.39 (*d*, 2.5)	103.7	2, 11b	6.48 (*d*, 2.4)	102.4	2, 11b
4a		157.0			156.5	
6	eq: 4.29 (*ddd*, 10.6, 4.6, 0.4) ax: 3.63 (d, 10.6)	66.1	4a, 11a, 6b, 6a	eq: 3.66 (*t*, 11.2) ax: 4.23 (*dd*, 4.8, 11.2)	66.5	4a, 6a, 6b, 11a
6a	3.69 (*m*)	39.3	6, 6b, 10a	3.48 (*ddd*, 1.6, 4.8, 6.4)	40.2	6, 6b, 10a
6b		110.0			117.9	
7		150.8		6.72 (*s*)	104.7	6a, 8, 9, 10a
8		135.7			141.7	
9		155.0			148.1	
10	6.21 (*s*)	90.8	8, 9, 6b, 10a	6.43 (*s*)	93.8	8, 9, 6b, 10a
10a		156.1			154.3	
11a	5.43 (*d*, 7.0)	78.4	1, 6 , 4a, 11b	5.49 (*d*, 7.2)	78.6	1, 6, 4a, 11b
11b		113.1			112.3	
7-OCH_3	3.96 (*s*)	61.0	7			
8-OCH_3	3.73 (*s*)	61.1	8			
9-OCH_3	3.77 (*s*)	56.3	9			
8/9-OCH_2O				5.89/5.92 (*d*, 1.6)	101.3	8, 9
1'				4.49 (*d*, 7.2)	64.9	3, 2', 3'
2'				5.47 (*m*)	119.4	4', 5'
3'					138.4	
4'				1.79 (*s*)	25.8	2', 3', 5'
5'				1.73 (*s*)	18.2	2', 3', 4'

tionalities is expected to influence only the short-wavelength part of the spectrum, while retaining the symmetry of its long-wavelength part at 288 nm. Overall, based on the NMR, CD and DFT data this compound was identified as (6a*R,* 11a*R*)-7,8,9-trimethoxy-3-hydroxypterocarpan (**1**), and was assigned the trivial name micanspterocarpan.

Column chromatographic separation of the CH_2Cl_2/CH_3OH (1:1) extract of the root bark of *Millettia dura* led to the isolation of a new pterocarpan (**2**, Figure **1**) along with seven known compounds (Figure **4**) that were identified as calopogonium isoflavone B (**3**) [18], isoerythrin A-4'-(3-methylbut-2-enyl) ether (**4**) [10,12], maximaisoflavone B (**5**) [9], durmillone (**6**) [10,18], 7,2'-dimethoxy-4',5'-methylenedioxyisoflavone (**7**) [9,

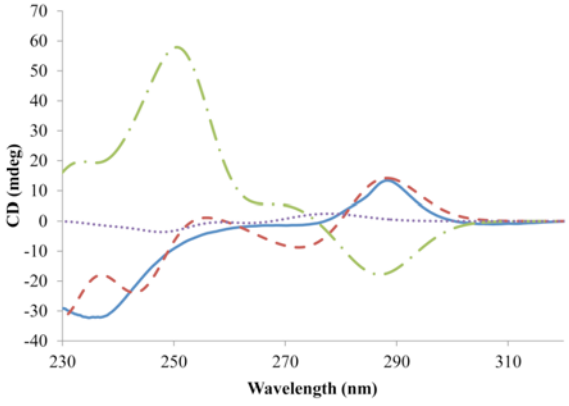

Figure 3: The CD spectra of **1**. Besides the experimental spectrum (——, blue), those computationally (DFT) predicted for the *cis*-fused 6a*R*,11a*R*-**1** (----, red), for the *cis*-fused 6a*S*,11a*S*-**1** (— · —, green) and for *trans* fused 6a*R*,11a*S*-**1** (····, purple) configurational isomers are shown.

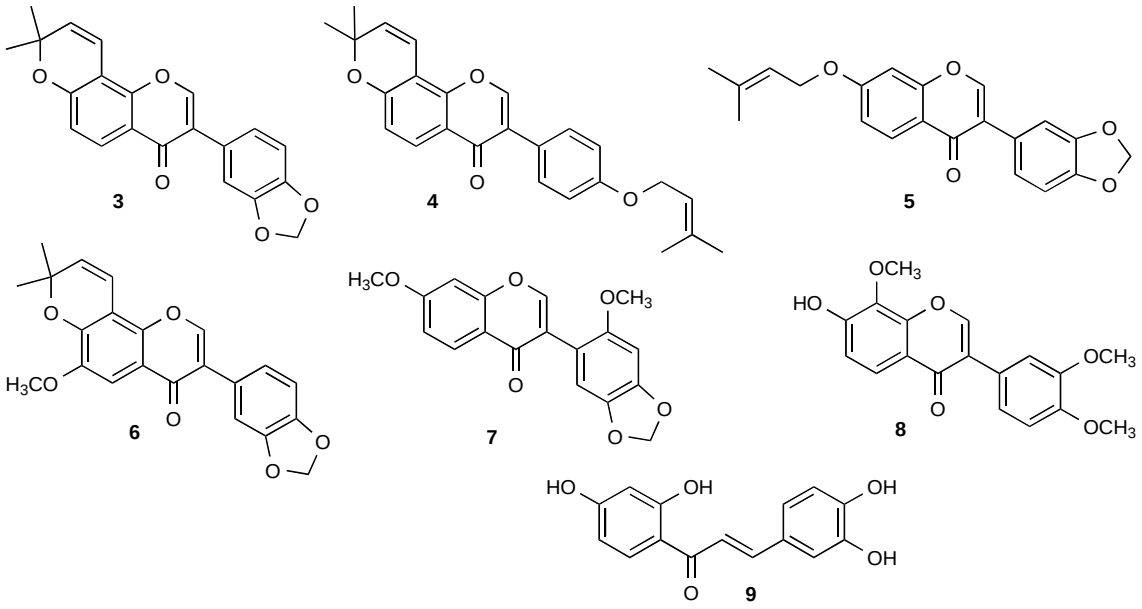

Figure 4: Calopogonium isoflavone B (**3**) [18], isoerythrin A-4'-(3-methylbut-2-enyl) ether (**4**) [10,12], maximaisoflavone B (**5**) [9], durmillone (**6**) [10,18], 7,2'-dimethoxy-4',5'-methylenedioxyisoflavone (**7**) [9,18], 7-hydroxy-8,3',4'-trimethoxyisoflavone (**8**) [19], and butein (**9**) isolated from the root bark of *Millettia dura*.

18], 7-hydroxy-8,3',4'-trimethoxyisoflavone (**8**) [19], and butein (**9**) [20] upon comparison of their spectroscopic data with those previously published.

Compound **2** was obtained as a colorless oil. Based on HRMS (ESI) analysis the molecular composition of **2** was suggested to be $C_{21}H_{20}O_5$ ($[M+H]^+$, *m/z* obs 353.1386, calcd 353.1311). The NMR data (Table **1**) showed high similarities to that of **1**, revealing that it also has a pterocarpan skeleton [13] having a prenyloxy (OCH_2-1', CH-2', CH_3-4', CH_3-5' and C-3') and a methylenedioxy (8/9-OCH_2O) substituent. For ring A, similar to **1**, an ABX spin system was observed with the signal at δ_H 7.39 assigned to H-1 upon observation of its HMBC correlations to C-3 (δ_c 160.3), C-4a (δ_c 156.5), and C-11a (δ_c 78.6). Connection of the prenyloxy group to C-3 was indicated by the NOE of CH_2-1' to H-2 (δ_H 6.64) and to H-4 (δ_H 6.48), and by the HMBC correlations of the CH_2-1' protons to C-3 (δ_c 160.3). The presence of two singlet aromatic protons, H-7 (δ_H 6.72) and H-10 (6.43), of ring D is consistent with the placement of the methylenedioxy group at C-8/9. *Cis* configuration of the B/C ring junction was indicated by the $^3J_{H\text{-}6a,H\text{-}11a}$=6.4 Hz, confirmed by the NOE observed between H-6a and H-11a. Based on the above information, and on the expected common biosynthetic route to **1**, this new compound was characterized as (6a*R*,*11a*R**)-3-*O*-prenylmaackiain (**2**).

The crude extract of the root bark of *M. dura* and some of its isolated constituents were tested for cytotoxicity against the MDB-MB-231 human breast cancer cell line (Table **2**), the HEK-293 human embryonic kidney cell line and the chloroquine resistant (Dd2) and chloroquine sensitive (3D7) strains of *Plasmodium falciparum*. As part of an ongoing screening for small molecule inhibitors of eukaryotic protein synthesis, the isolated constituents were also tested in Krebs-2 *in vitro* translation extracts programmed with a bicistronic firefly-HCV IRES-Renilla luciferase mRNA construct, to simultaneously monitor cap-dependent and cap-independent translation [21]. Minimal antiplasmodial activity was observed for compounds **3**-**5** and **7** against the chloroquine sensitive 3D7 and the chloroquine resistant Dd2 *P. falciparum* strains; demonstrating activities between 70-90% inhibition at 40 μM. Among the compounds tested, **5** and **7** showed low toxicities against the Estrogen receptor (ER) negative MDB-MB-231 breast cancer cells. None of the compounds showed translation inhibitory activity *in vitro* or cytotoxicity against the HEK-293 human embryonic kidney cell line, up to 40 μM concentration.

Table 2: Cytotoxic Activities of the Crude Extract of Root Bark of *Millettia dura* and Some of its Isolated Constituents Against MDB-MB-231

Sample	IC_{50}, µM
Crude extract of root bark of *M*. *dura**	31.7
Calopogonium isoflavone B (3)	> 287.3
Isoerythrin A-4'-(3-methylbut-2-enyl) ether (4)	> 257.6
Maximaisoflavone B (5)	153.5
7,2'-Dimethoxy-4',5'-dimethylenedioxy-isoflavone (7)	174.1

*IC_{50} for the crude extract is given in µg/ml.

EXPERIMENTAL SECTION

General

Melting points were obtained on a Büchi Melting point B-545 instrument. NMR spectra were acquired on Bruker Avance III 600 (^{1}H: 600.25 MHz; ^{13}C: 150.95 MHz) and Bruker Avance III HD 800 (^{1}H: 799.87 MHz, ^{13}C: 201.15 MHz) spectrometers. All spectra were processed using MestReNova 10.0 using the residual solvent peak as indirect chemical shift reference. HRMS (EI) spectra were obtained on a Micromass GC-TOFmicro mass spectrometer (Micromass, Wythenshawe, Waters Inc., UK), using direct inlet and 70 eV ionization voltage. LC-MS (ESI) chromatograms were acquired on a Perkin-Elmer PE SCIEX API 150EX instrument equipped with a Turbolon spray ion source connected to a Gemini 5 mm RPC_{18} 110 Å column, applying a H_2O/MeCN 80:20-20:80 gradient with a separation time of 8 minutes. TLC was carried out on Merck pre-coated silica gel 60 F254 plates. Gel filtration was done on Sephadex LH-20. Preparative HPLC was carried out on a Waters 600E instrument using the Chromulan (Pikron Ltd) software and an RP C8 Kromasil® (250 mm x 55 mm) column with a H_2O/CH_3OH solvent system.

Plant Materials

The root bark of *Millettia dura* was collected from Mulathankari, Meru County, Kenya in the year 2013. The plant material was identified by Mr. Patrick Chalo Mutiso of the School of Biological Sciences, University of Nairobi, Kenya and the specimen was deposited at the Herbarium of the School of Biology with voucher number TD-2013/03. The root bark of *Millettia micans* was collected from Kisarawe-Tanzania and was identified by Mr. F. Mbago of the Department of Botany, University of Dar es Salaam. A voucher specimen (FMM 3591/ 2013) was kept at the Institute of traditional medicine, Muhimbili University of Health and Allied Science, Tanzania.

Extraction and Isolation of Compounds from the Root Bark of *Millettia micans*

The dried and ground root bark (1 kg) of *Millettia micans* was extracted with CH_2Cl_2/CH_3OH, (1:1) exhaustively, three times for 24 hours each. The extracts were filtered and concentrated using a rotary evaporator to give a brown crude extract (38 g). A 3.5 g portion of the crude extract was subjected to column chromatography on silica gel (150 g) and was eluted with the mixture of *n*-hexane and EtOAc with increasing polarities. The fractions, which were eluted with 6% EtOAc in *n*-hexane yielded compound **1** (40.4 mg) on purification by Sephadex LH-20, and were subsequently recrystallized from *n*-hexane/CH_2Cl_2.

Extraction and Isolation of Compounds from the Root Bark of *Millettia dura*

The air-dried and ground root bark (1.5 kg) of *Millettia dura* was extracted with CH_2Cl_2/CH_3OH (1:1), as described above. The solvent of the extract was removed using a rotary evaporator to give 100 g of a light brown crude extract. A portion of the crude extract (90 g) was subjected to column chromatography on silica gel eluted with *n*-hexane containing increasing amounts of EtOAc. The fractions collected from 2% EtOAc in *n*-hexane were combined and separated on Sephadex, LH-20 (CH_2Cl_2:CH_3OH, 1:1) to give compound **2** (1.5 mg), which was further purified on

HPLC using CH_3OH:H_2O gradient. The post fractions of 2% EtOAc in *n*-hexane were combined and subjected to column chromatography on silica gel using *n*-hexane and EtOAc (4:1) to give calopogonium isoflavone B (**3**, 140.9 mg), maximaisoflavone B (**5**, 23.6 mg) and impure isoerythrin A-4'-(3-methylbut-2-enyl) ether (**4**). The purification of **4** (6.8 mg) was achieved by reverse-phase preparative HPLC using a CH_3OH:H_2O gradient. Durmillone (**6**, 7.4 mg) was obtained from 6% EtOAc in *n*-hexane elution through crystallization in CH_3OH. The fractions eluted with 8-10% EtOAc were combined and subjected to column chromatography using *n*-hexane/EtOAc (4:1) to give 7,2'-dimethoxy-4',5''-methylenedioxyisoflavone (**7**, 156.6 mg). Similarly, 7-hydroxy-8,3',4'-trimethoxyisoflavone (**8**, 7.1 mg) was obtained as a colorless solid from the fraction eluted with 12-15% EtOAc in *n*-hexane on a silica gel column. The fractions eluted with 25-30% EtOAc in *n*-hexane were combined and applied on Sepahedex LH-20 using a CH_2Cl_2/CH_3OH 1:1 mixture to give butein (**9**, 2.70 mg).

Physical and Spectroscopic Data of 1 and 2

Micanspterocarpan (**1**)*.* White amorphous powder. UV λ_{max} (CH_3OH) 268, 281 nm. $[\alpha]_D$-134.3^0 (CH_2Cl_2, *c* 21.5 mg/100ml). CD: (CH_3OH, Figure **3**); ^{1}H and ^{13}C NMR, see Table **1** and Supporting Information; MS (EI, 70 ev) (rel. int.) *m/z* 330 (100, $[M]^+$), 315 (32, M-Me]$^+$, 157 (25), 147 (31), 131 (41), 123 (41); HRMS (EI) *m/z* obs 330.1115 $[M]^+$, calcd 330.1103 ($C_{18}H_{18}O_6$).

3-O-Prenylmaackiain (**2**). Colorless oil. ^{1}H and ^{13}C NMR, see Table **1** and Supporting Information; MS (ESI) *m/z* 353.6 $[M+H]^+$; HRMS (ESI) *m/z* obs 353.1386, calcd 353.1311 ($C_{21}H_{20}O_5$).

Theoretical Calculations

Geometries were optimized at the B3LYP/6-311G** [23,24] level of theory without constraints. CD spectra were computed using the Time Dependent DFT (TDDFT) [25,26] algorithm encompassed into the program package GAUSSIAN 09 [27] applying the 6-31G* basis set. For spectra prediction 15 singlet and 15 triplet states were solved using the keyword "TD" with Nstates=15, 50-50. All GAUSSIAN results were analysed and the spectra were displayed using the SpecDis 1.62 software [28]. Different conformations were weighted according to their Boltzmann distribution. Molecules were displayed using SYBYL-X 2.1.1 [29].

Cytotoxicity Assays

MDB-MB-231 human breast cancer cells were cultured in Dulbecco's modified eagle medium (DMEM), supplemented with 10% (v/v) fetal bovine serum, 2 mM L-glutamine, 100 units/ml penicillin and 100 µg/ml streptomycin at 37 °C in humidified 5% CO_2. For cytotoxicity assays, cells were seeded in 96-well plates at optimal cell density (10^4 cells per well) to ensure exponential growth for the duration of the assay. After a 24 h pre-incubation period, the medium was replaced with experimental medium containing the appropriate compound concentrations or vehicle controls (0.1% or 1.0% v/v DMSO). After 72 h incubation, cell viability was measured using Alamar Blue (Invitrogen Ab, Lidingö, Sweden) according to the manufacturer's instructions. Absorbance was measured at 570 nm with 600 nm as a reference wavelength. Results were expressed as the mean ± standard error for six replicates as a percentage of vehicle control (taken as 100%). Experiments were performed independently at least six times. Statistical analyses were performed using a two-tailed Student's t-test. $P < 0.05$ was considered to be statistically significant.

To assess the cytotoxicity of compounds on HEK-293 cells in dose response, a resazurin-based viability assay was used. In brief, HEK-293 cells were grown in DMEM medium (Life Technologies), containing 10% fetal calf serum (FCS; Gibco), trypsinised, counted and seeded at 2000 cells per well in 45 µL media into TC-treated 384-well plates (Greiner) and left to adhere overnight at 37 °C, 5% CO_2 and 95% humidity. Test compounds were prepared by diluting compounds 1 in 25 in sterile water and then another 1 in 10 dilution, to give a top final test concentration of 40 µM, 0.4% DMSO. Plates were incubated for 72 h at 37 °C, 5% CO_2 and 95% humidity, and then the media was removed and replaced by 35 µL of 44 µM resazurin in DMEM without FCS. The plates

were incubated for another 4-6 h at 37°C, 5% CO_2 and 95% humidity, before reading on an EnVision® Plate Reader (PerkinElmer) using fluorescence excitation/emission settings of 530 nm/595 nm. The % growth was standardized to controls (40 µM puromycin as positive and 0.4% DMSO as negative control) using Microsoft® Excel 2013. A statistical analysis including IC_{50} determination and graphical output was performed in GraphPad Prism® 6 using nonlinear regression variable slope curve fitting.

Plasmodium falciparum Culture

In vitro parasite culture of the *P. falciparum* strains 3D7 and Dd2 were maintained in RPMI with 10 mM Hepes (Life Technologies), 50 µg/mL hypoxanthine (Sigma) and 5% human serum from male AB plasma and 2.5 mg/mL AlbuMAX II® (Life Technologies). Human 0+ erythrocytes were obtained from the Australian Red Cross Blood Service (Agreement No: 13-04QLD-09). The parasites were maintained at 2-8% parasitaemia (% P) at 5% haematocrit (% H), and incubated at 37 °C, 5% CO_2, 5% O_2, 90% N_2 and 95% humidity.

Plasmodium falciparum Growth Inhibition Assay

A previously developed, well-established asexual *P. falciparum* imaging assay was used to determine parasite growth inhibition according to the procedure described by Duffy, and Avery [30].

Translation Inhibitory Assay

A previously developed assay [21] was used to measure the translation inhibitory activity of the studied compounds. The compounds were suspended at a concentration of 10 mM in DMSO and subsequently diluted to 200 µM in water. They were tested at a final concentration of 20 µM in Krebs-2 translation extracts programmed with a bicistronic Firefly-HCV IRES-Renilla luciferase mRNA construct. Translation reactions were incubated at 30°C for 60 min at which point the luciferase activities were then measured. Compounds that inhibit only FF would be considered cap-dependent translation inhibitors, compounds that inhibit expression of Ren only would be inhibitors of HCV IRES translation while compounds that inhibit both FF and Ren would likely be translation elongation inhibitors. None of the compounds were observed to display significant inhibition of translation.

CONCLUSIONS

Two new pterocarpans were identified from the CH_2Cl_2/CH_3OH (1:1) root bark extracts of *Millettia micans* and *Millettia dura*, along with seven known compounds from the latter extract. Marginal antiplasmodial activity was observed for calopogonium isoflavone B (**3**), isoerythrin A-4'-(3-methylbut-2-enyl) ether (**4**), maximaisoflavone B (**5**) and 7,2'-dimethoxy-4',5'-methylenedioxyisoflavone (**7**) against the chloroquine sensitive (3D7) and resistant (Dd2) strains of *Plasmodium falciparum*. Whereas **5** and **7** showed some toxicity against the MDB-MB-231 human breast cancer cell line at high concentrations, **3** and **4** were inactive. None of the isolated compounds showed toxicity against the HEK-293 human embryonic kidney cell line, and they lacked translation inhibition potency.

ACKNOWLEDGMENTS

We are grateful to Mr. P. C. Mutiso of the Herbarium, School of Biological Sciences, University of Nairobi and Mr. F. Mbago, the botanist from the Department of Botany, University of Dar es Salaam, for the identification of the plant species for this study. M.M. and T.D. are grateful to the Natural Products Research Network for Eastern and Central Africa (NAPRECA) and the German Academic Exchange Service (DAAD) for a scholarship. The Swedish Research Council (Swedish Research Links, 2012-6124), the International Science Program (ISP Sweden, grant KEN-02) and the Australian Research Council (Grant LP120200557 to VMA) are thankfully acknowledged for financial support. We thank the Australian Red Cross Blood Service for the provision of human blood.

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Received On: 13-August-2015 Accepted On: 12-October-2015 Published On: 05-January-2016