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PII: S0040-4039(17)31114-0
DOI: http://dx.doi.org/10.1016/j.tetlet.2017.09.005
Reference: TETL 49275

To appear in: *Tetrahedron Letters*

Received Date: 31 July 2017
Revised Date: 30 August 2017
Accepted Date: 4 September 2017

Please cite this article as: Kumar, V., Gupta, M., Gandhi, S.G., Bharate, S.S., Kumar, A., Vishwakarma, R.A., Bharate, S.B., Anti-inflammatory chromone alkaloids and glycoside from *Dysoxylum binectariferum* ‖, *Tetrahedron Letters* (2017), doi: http://dx.doi.org/10.1016/j.tetlet.2017.09.005

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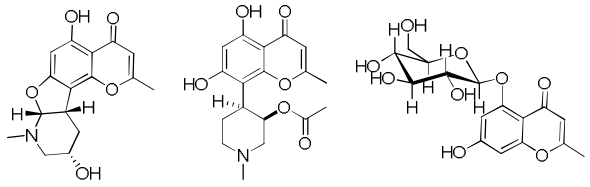

Chrotacumine E (**6**) First report from this genus

Chrotacumine K (**12**) (new)

Schumaniofioside A (**13**) First report from this genus

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Tetrahedron Letters
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Anti-inflammatory chromone alkaloids and glycoside from *Dysoxylum binectariferum*[‖]

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ARTICLE INFO

Article history:
Received
Received in revised form
Accepted
Available online

Keywords:
chrotacumine K,
rohitukine,
schumaniofioside A,
chromone alkaloid,
anti-inflammatory,
Dysoxylum binectariferum

ABSTRACT

Herein we report isolation of a new chromone alkaloid chrotacumine K (**12**) from fruits and a chromone glycoside schumaniofioside A (**13**) from leaves of *Dysoxylum binectariferum* Hook f. Schumaniofioside A is reported for the first time from Meliaceae family. Other known alkaloids isolated include rohitukine (**1**) and chrotacumine E (**6**). The structure of new alkaloid **12** was elucidated on the basis of extensive 1D and 2D NMR analysis, synthesis and chemical hydrolysis. Chemically, chrotacumine K (**12**) is a 3´-*O*-acetyl rohitukine which on chemical or enzymatic hydrolysis produces rohitukine. The new alkaloid **12** is also present in seeds and stem-barks of this plant. The glycoside schumaniofioside A (**13**) is present only in leaves, and in abundance (~1% w/w of dried leaves). The isolated compounds and extracts were evaluated for *in-vitro* effect on the proinflammatory cytokines (TNF-α and IL-6) in human monocytic THP-1 cells. The alkaloid **12** displayed potent inhibition (57%) of TNF-α at 0.3 µM, and was non-toxic to THP-1 cells up to 40 µM, indicating its excellent therapeutic window. Furthermore, a nitrobenzoyl ester analog **3e** showed better inhibition of IL-6 than parent natural product chrotacumine K.

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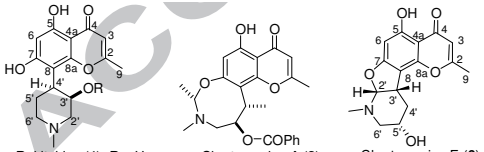
Dysoxylum species is a rich source of chromone alkaloids. The widely investigated natural product rohitukine (**1**)[1] has been isolated from barks of *Dysoxylum binectariferum* Hook (Meliaceae)[2] and is reported to possess a wide range of biological activities including cytotoxicity,[3] antidyslipidemic,[4] antiadipogenic,[5] gastroprotective,[6] antifertility[7] and antileishmanial activity.[8] Furthermore, this natural product has inspired the discovery of two anticancer clinical candidates flavopiridol[9-10] and P276-00.[11] The structural variations on rohitukine in nature was primarily observed as change in the location of piperidinyl moiety from 8th to 6th position (dysoline)[12] and substitution of piperidine hydroxyl with acyl units, a class of compounds called chrotacumines A-J (**2-11**).[13-16] (Figure 1).



Chrotacumine B (**3**): R = - COC(Me)=CH-Me
Chrotacumine C (**4**): R = -COPh(3,4,5-tri-OMe)
Chrotacumine D (**5**): R = -COPh(3,4-di-OMe)
Chrotacumine F (**7**): R = -CO-CH=CH-Ph
Chrotacumine G (**8**): R = -CO-CH=CH-Ph (3,4,5-tri-OMe)
Chrotacumine H (**9**): R = -CO-CH=C(Me)CH(CH$_3$)$_2$
Chrotacumine I (**10**): R = -COPh(3,5-di-OMe,4-OH)
Chrotacumine J (**11**): R = -COPh(3-OMe,4-OH)

Figure 1. Structures of rohitukine (**1**) and chrotacumines A-J (**2-11**)

Chrotacumine A and E has modified piperidinyl ring; whereas rest all chrotacumines are 3'-*O*-acyl derivatives of rohitukine. Amongst all 3'-*O*-acyl rohitukine derivatives, most of them are benzoyl derivatives and few are with 3-5 carbon chain containing aliphatic acyl units; however simple 3'-*O*-acetyl-rohitukine has never been reported in the literature.

During our efforts to explore fruits and leaves of *Dysoxylum binectariferum* as an alternative (renewable) source of rohitukine isolation; a new alkaloid chrotacumine K (3'-*O*-acetyl-rohitukine) along with chrotacumine E, schumaniofioside A and rohitukine have been isolated and characterized. Herein, we are reporting for the first time isolation of schumaniofioside A from Meliaceae family. Previously, it was reported from *Pancratium maritimum, Schumanniophyton magnificum* and *Staphylea bumalda* (DNP search). The chemical structures of newly isolated chrotacumine K (**12**), and schumaniofioside A (**13**) are shown in Figure 2. The bioactivity evaluation of isolated compounds for inhibition of proinflammatory cytokines was also performed.

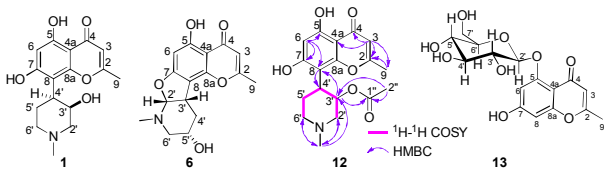


Figure 2. Chromone alkaloids **1, 6, 12** and chromone glycoside **13** isolated from *D. binectariferum*. The key COSY and HMBC correlations of chrotacumine K (**12**) are also shown.

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[‖]IIIM Publication Number. IIIM/1933/2016

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The HPLC chromatogram of methanolic extract of *Dysoxylum binectariferum* fruits[17] showed three key peaks at t_R 11.5, 12.7 and 17.5 min, respectively (Figure 3a). The co-TLC with reference standard available in our laboratory indicated that the peak at 11.5 min belongs to rohitukine; however the peak at t_R 12.7 min appeared to be the new one. The methanolic extract was loaded on silica gel column and was eluted with increasing concentration of methanol in chloroform. At 7-8% methanol in chloroform, a new alkaloid was isolated followed by isolation of rohitukine at 12-13% methanol in chloroform. Isolated compounds were characterized by NMR and MS analysis.[18] Rohitukine was characterized by co-TLC with reference standard and by comparison of their spectral data with literature values.[1] The NMR of new alkaloid was recorded in $CDCl_3$ (in order to see phenolic OH signals) as well as CD_3OD (for comparison with rohitukine).

The alkaloid **12** showed dragendorff positive test, and its ^{1}H NMR spectra was similar (except few differences) to rohitukine, which gave indication that it could be a rohitukine class of compound. In the ^{1}H NMR spectrum of **12**, the signal at δ 4.14 ppm (H-3′) of rohitukine was downfield-shifted to δ 5.18 ppm. Similarly, in the ^{13}C NMR, the signal at *δ* 66.70 ppm (C-3′) of rohitukine was shifted to δ 71.14 ppm. The ^{13}C NMR also showed the presence of two extra carbons, one at δ 170.6 ppm and other at δ 21.01 ppm. These observations clearly indicated the presence of acetyl group at 3'-OH. The presence of ester group was also confirmed by IR spectra with appearance of stretching vibration at 1737 cm^{-1}. Furthermore, the position of acetyl ester at 3′ position of piperidine ring was ascertained by HMBC studies, wherein a key correlation between H-3′ with C-7′ was observed. The key HMBC correlations of compound **12** are shown in Figure 2.

It is worth reporting that when compound **12** was submitted for NMR studies in CD_3OD and after checking TLC of the sample after a week, the portion of the **12** was converted to rohitukine (**1**). Furthermore, the HPLC analysis of the methanolic extract of fruits recorded immediately on preparation and after a month indicated that the ratio of rohitukine to chrotacumine K get changed, with significantly increased percentage of rohitukine. The HPLC comparison of rohitukine, chrotacumine K and partially hydrolyzed chrotacumine K is shown in Figure 3b-c. The ^{1}H and ^{13}C NMR assignments of chrotacumine K (**12**) along with rohitukine and its closely related chrotacumine H are shown in Table 1. Further, the presence of chrotacumine K in chloroform and water extracts of fruits of *D. binectariferum* was investigated. Chrotacumine K was present in both these extracts (HPLC chromatograms are depicted in Section S36 of supporting information). The presence of this compound was also investigated in seeds, stem-bark and leaves of *D. binectariferum* by TLC and HPLC analysis. The seeds, stem-barks and leaves of *D. binectariferum* were extracted with chloroform. The co-TLC of these chloroform extracts with chrotacumine K indicated its presence in seeds and stem-barks; however it was found absent in leaves (TLC images are shown in section S14 of supporting information). HPLC analysis also supported these observations. Next, the chrotacumine K (**12**) was synthetically prepared by reacting rohitukine with acetyl chloride in presence of triethylamine (Figure 4). The synthesized 3′-*O*-acetyl rohitukine and isolated chrotacumine K were identical in all respects *viz.* TLC, HPLC, and NMR.

From the methanolic extract of seed, another dragendorff positive compound was isolated, but in very minor amount (5 mg). On TLC analysis, it was found non-polar to both rohitukine and chrotacumine K. After comparison of spectral data with literature values, it was identified as chrotacumine E (**6**).[14] The comparison of ^{1}H and ^{13}C NMR values of chrotacumine K (**12**) with rohitukine, chrotacumine E and chrotacumine H is shown in Table 1.

Our observations indicated that the conversion of chrotacumine K into rohitukine is a slow process; and the extraction process involved cold maceration for 2 hrs. Therefore, there would be conversion of very small amount of chrotacumine K to rohitukine during extraction. But still, the ratio between chrotacumine K and rohitukine that we observed during extraction (as depicted in Figure 3a) may not be the real ratio of them in fruits.

During phytochemical efforts on leaves of *D. binectariferum*, it was interesting to observe that the HPLC chromatogram of hydroalcoholic extract of leaves showed presence of only two peaks, of equal intensity. The first among these two peaks was rohitukine, whereas the second peak was observed to be unknown, as its HPLC and TLC profile does not matched with any of the reference

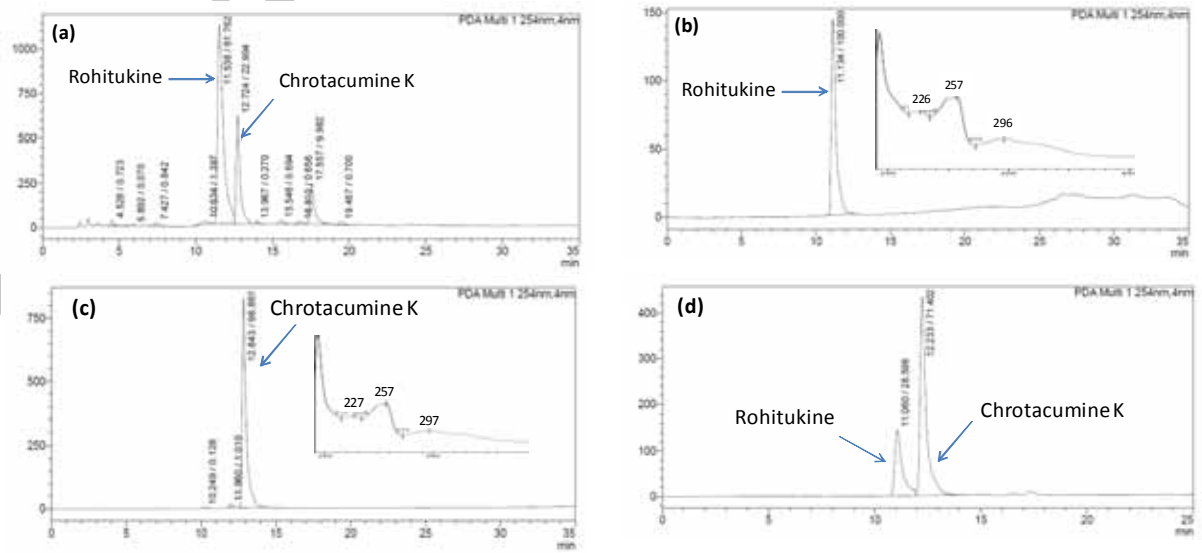

Figure 3. HPLC chromatogram of (a) fruits of *D. binectariferum* MeOH extract; (b) rohitukine; (c) chrotacumine K; and (d) chrotacumine K hydrolysis to rohitukine in CD_3OD. Insets in Figure 2b and 2c are UV chromatograms of respective compounds.

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Table 1. The ^{1}H and ^{13}C NMR assignments of chrotacumine K (**12**), chrotacumine E (**6**), rohitukine (**1**)[a] and schumaniofioside A (**13**)[b] and chrotacumine H (**9**)

Position	**12** in $CDCl_3$		**12** in CD_3OD		**6** in $CDCl_3$		**1** in CD_3OD		**13** in $CD_3OD/(CD_3)_2CO$		**9** in CD_3OD[c]	
	δ(H)	δ(C)	δ(H)	δ(C)	δ(H)	δ(C)	δ(H)	δ(C)	δ(H)	δ(C)	δ(H)	δ(C)
2	-	166.35	-	168.87	-	165.70	-	167.70	-	167.17 / 165.69	-	168.3
3	6.01	108.13	5.99	108.71	6.03	108.61	5.97	107.40	6.03 / 5.87	111.65 / 111.77	5.97	108.2
4	-	182.76	-	184.31	-	182.20	-	183.00	-	180.34 / 178.31	-	184.0
4a	-	104.43	-	106.44	-	104.45	-	104.00	-	109.19 / 109.78	-	104.2
5	-	160.79		161.93	-	160.36	-	160.70	-	160.16 / 160.19	-	161.6
5-OH	12.86	-	-	-	12.63	-	-	-	-/-	-	-	-
6	6.27	99.65	6.13	99.87	6.31	98.48	6.15	99.40	6.79 / 6.82	104.59 / 105.94	6.18	100.7
7	-	162.71	-	164.37	-	162.46	-	163.00	-	164.68 / 163.33	-	167.3
8	-	105.23	-	105.17	-	99.36	-	106.40	6.54 / 6.50	99.13 / 99.41	-	107.6
8a	-	156.81	-	158.30	-	155.08	-	156.50	-	161.11 / 160.29	-	158.7
9	2.38	20.42	2.34	20.38	2.36	20.15	2.32	18.90	2.33 / 2.20	19.88 / 19.78	2.44	20.5
2´	3.15-3.20	58.60	3.07- 3.17	57.59	4.96	86.51	3.49, 3.38	60.40	4.82 / 4.58	105.04 / 106.62	3.03, 2.45	60.6
3´	5.18	71.14	5.06	71.90	3.64-3.65	29.22	4.14	66.70	3.61-3.63	74.55 / 74.86	5.18	71.3
4´	3.53-3.56	35.71	3.42-3.46	37.55	1.94-2.00 2.07-2.15	27.29	3.62-3.59	35.70	3.46-3.48	77.30 / 77.19	3.52	37.9
5´	2.24-2.30, 1.81	24.81	3.17-3.07, 1.71	25.72	4.19-4.23	69.77	3.15, 1.75	21.90	3.43-3.46	71.30 / 71.37	3.24, 1.71	26.4
6´	3.15-3.20, 2.49	56.19	3.07-3.17, 2.53	59.88	2.07-2.15 2.81-2.85	51.97	3.35, 3.22-3.20	55.40	3.48-3.51	78.68 / 78.42	3.08, 2.20	58.0
7´	-	-	-	-	-	-	-	-	3.76-3.79, 3.95-3.98	62.53 / 62.92	-	-
1´´	-	170.60	-	172.12	-	-	-	-	-	-	-	167.9
2´´	1.88	21.01	1.80	20.93	-	-	-	-	-	-	5.63	114.4
3´´	-	-	-	-	-	-	-	-	-	-	-	167.0
4´´	-	-	-	-	-	-	-	-	-	-	2.29	39.1
5´´	-	-	-	-	-	-	-	-	-	-	1.02	21.2
6´´	-	-	-	-	-	-	-	-	-	-	1.01	21.3
7´´	-	-	-	-	-	-	-	-	-	-	1.86	16.6
N-CH_3	2.38	45.93	2.35	46.01	2.55	41.52	2.82	42.90	-	-	2.32	46.5

[a] the ^{1}H and ^{13}C NMR of chrotacumine K was recorded in $CDCl_3$ as well as CD_3OD; however NMR of rohitukine was recorded only in CD_3OD (as rohitukine was insoluble in $CDCl_3$). [b] the ^{1}H and ^{13}C NMR of schumaniofioside A (**13**) was recorded in CD_3OD as well as in $(CD_3)_2CO$ in order to see the presence of OH group at carbon no C5. [c] data taken Morita *et al.,* 2014.[13]

standards present with us. It does not showed Dragendorff positive test, indicating that it is not a alkaloid. The ^{1}H, ^{13}C NMR, COSY, HMBC and NOESY correlations were recorded, which revealed that it to be a schumaniofioside A, a chromone-5-*O*-glycoside.[19] The key COSY, HMBC and NOESY correlation are shown in Section S37 of supporting information. The chemical hydrolysis was performed, in order to know the identity of aglycone and glycone as noreugenin and β-D-glucose, respectively. Schumaniofioside A was found to be present in 3-5% w/w in the extract of leaves (i.e. ~1% w/w in dried leaves). Young aged leaves were found to have higher schumaniofioside A content compared to older leaves. The HPLC chromatogram of hydroalcoholic extract of leaves is provided in section S37 of supporting information.

Further, in order to establish preliminary SAR for rohitukine esters for cytokine inhibition activity, a series of rohitukine-3-O-esters **3a-f** (chrotacumine K analogs) were prepared (Figure 4). All prepared esters were characterized by NMR, mass and IR spectroscopy and details are provided in the supporting information.

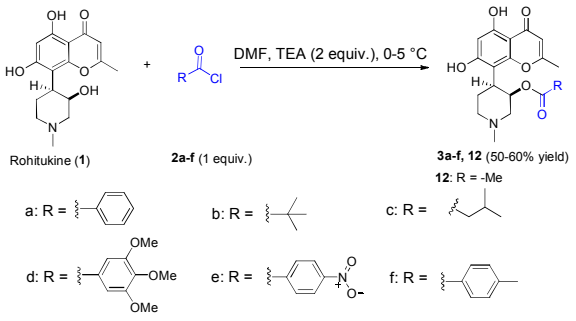

Figure 4. Synthesis of chrotacumine K (**12**) and its ester analogs **3a-f**

Dysoxylum binectariferum and its reported constituents have been reported to possess anti-inflammatory activity.[12,20] Therefore, the effect of isolated compounds and crude extract on inhibition of proinflammatory cytokines TNF-α and IL-6 in THP-1 cells[21] was investigated; and results are shown in Table 2. THP-1 cells were stimulated for release of cytokines by LPS. After treatment of LPS-treated cells with test samples, the cytokine levels were measured. The methanolic extract of fruits (DBFM ext) and hydroalcoholic extract of leaves (DBLHA ext) showed promising inhibition (43-60% inhibition) of both cytokines (TNF-α and IL-6) at 2.5-3.12 µg/ml. Rohitukine at 5 µM, showed 50 and 82% inhibition of TNF-α and IL-6, respectively. A newly isolated alkaloid **12** showed potent inhibition of TNF-α; and a moderate inhibition of IL-6, at 10 µM,

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while chrotacumine E (**6**) and schumaniofioside A (**13**) showed moderate inhibition of both cytokines. In case of synthesized esters, varying degree of cytokine inhibition was observed and results are included in Table 3. All the synthesized esters except compound **3f** showed good TNF-α inhibition. The compound **3e** (*p*-nitro-phenyl ester derivative) showed comparatively better inhibition of both the cytokines compared to all isolated natural compounds. Compound **3e** inhibited cytokine IL-6 level up to 91% at 10 µM. Because of the promising cytokine inhibition activity of compound **3e** and chrotacumine K (**12**), the concentration-dependent inhibition of IL-6 by compound **3e** while the concentration-dependent inhibition of TNF-α by MeOH extract and chrotacumine K (**12**) was studied and results are shown in section S38 of supporting information. All of them showed concentration-dependent effect on cytokines.

Since this bioactivity is performed in a cell based assay, the compound should remain intact in the buffer solution (in fact, the stability of **12** was studied in PBS pH 7.2 and compound was found to be stable up to 24 hrs). Therefore, it is speculated that esters remain intact and play a role in the activity in *in-vitro* assay.

Next, the cytotoxic effect of DBFM extract, compound **12** and **3e** was assessed on the THP-1 cells. For toxicity evaluation, seven different concentrations were used *viz*. 0.625, 1.25, 2.5, 5, 10, 20 and 40 µM. Similarly, concentrations 0.625, 1.25, 2.5, 5, 10, 20 and 40 µg/ml were used for fruit extract. The results of cell viability assay indicated that neither extract *nor* compounds **12** and **3e** showed any toxicity to the THP-1 macrophages at tested concentrations. Results are shown in Section S39 of supporting information.

Table 2. Inhibition of proinflammatory cytokines TNF-α and IL-6 by extracts of *D. binectariferum*, rohitukine (**1**), chrotacumine E (**6**), chrotacumine K (**12**) and schumaniofioside A (**13**) in THP-1 cells

Entry	% inhibition ± SD	
	TNF-α	IL-6
DBFM ext, 2.5 µg/ml	48.33 ± 2.34	43.11 ± 0.78
DBLHA ext, 3.12 µg/ml	52.18 ± 3.25	60.74 ± 0.42
Rohitukine (**1**), 5 µM[b]	50.60 ± 1.25	82.59 ± 1.62
Rohitukine (**1**), 10 µM[b]	41.74 ± 2.01	86.47± 2.01
Chrotacumine E (**6**), 10 µM	33.17 ± 1.09	16.01 ± 1.06
Chrotacumine K (**12**), 10 µM	81.09 ± 0.98	20.45 ± 2.20
Schumaniofioside A (**13**), 5 µM	39.51 ± 1.21	22.21 ± 0.58
Schumaniofioside A (**13**), 10 µM	41.40 ± 2.01	23.57 ± 1.18

Table 3. Inhibition of proinflammatory cytokines TNF-α and IL-6 by chrotacumine K ester analogs **3a-f** in THP-1 cells

Entry	% inhibition ± SD			
	TNF-α		IL-6	
	1 µM	10 µM	1 µM	10 µM
3a	35.12 ± 1.57	75.63 ± 2.81	24.11 ± 0.21	10.31 ± 1.23
3b	48.22 ± 1.43	49.36 ± 0.14	28.20 ± 1.73	23.10 ± 2.13
3c	44.45 ± 3.12	62.10 ± 2.31	35.01 ± 0.72	16.41 ± 1.34
3d	35.08 ± 2.89	45.78 ± 1.81	20.78 ± 2.01	26.31 ± 0.80
3e	nd	79.06± 1.78[a]	70.31 ± 0.56	91.29 ± 1.87
3f	32.02 ± 3.02	32.65 ± 1.30	26.21 ± 1.78	23.20 ± 1.23
12	55.76 ± 1.23	81.09 ± 0.98	nd	20.45 ± 2.20

[a] compound **3e** was tested at 5 µM for TNF-α inhibition; nd: not determined

The physicochemical properties are very crucial for any bioactive compound to move ahead in preclinical studies. Therefore, as a preliminary step towards this, we determined the aqueous solubility,[22] lipophilicity (log P)[23] and distribution co-efficient (log D)[23] of chrotacumine K along with rohitukine and schumaniofioside A. Results are shown in Table 4. Chrotacumine K showed excellent aqueous solubility. The Log P and Log D values were slightly towards more polar side (deviating from the acceptable drug-like properties). Aqueous solubility of schumaniofioside A was found to be 2.08 mg/ml. The stability of chrotacumine K in rat plasma was also studied, in order to understand whether it gets hydrolyzed to the rohitukine under enzymatic conditions. It was observed that after 4 h of incubation of compound in rat plasma, 80% of the chrotacumine was converted to rohitukine. This is indicative of the fact that in *in-vivo* efficacy studies, chrotacumine K will act as a prodrug of rohitukine (which is a bioactive natural product).

Table 4. Aqueous solubility, log P and log D of rohitukine (**1**), chrotacumine K (**12**) and Schumaniofioside A (**13**)[a]

Parameters	1	12	13
Solubility in water (mg/ml)	>10	> 10	2.081±0.176
Log P (water/ *n*-octanol)	–1.102 ± 0.063	0.413± 0.020	–0.447±0.0314
Log D (PBS pH 7.4/ *n*-octanol)	–0.414 ± 0.098	0.588 ± 0.016	–0.846±0.007

[a] values are shown as average of three independent determinations (± SD)

In summary, we have isolated a new chromone alkaloid chrotacumine K along with three known compounds chrotacumine E, schumaniofioside A and rohitukine from the fruits/seeds/leaves of *Dysoxylum binectariferum.* Schumaniofioside A was isolated for the first time from Meliaceae family and reported carbon assignments was corrected on the bases of 2D-NMR spectroscopy. Chrotacumine K was found present in other parts of this plant including seeds and stem barks. The newly isolated compound **12** displayed promising inhibition of pro-inflammatory cytokines, indicating its promise as an anti-inflammatory agent. Synthetic analog of chrotacumine K **3e** was found to be better inhibitor of cytokine IL-6 than parent natural product **12**. Both chrotacumine K and compound **3e** were found safe (*non-toxic*) to the THP-1 cells up to 40 µM, indicating their excellent therapeutic window.

Supporting information available. Experimental procedures and spectral data scans. This material is available free of charge via the internet at http://sciencedirect.com.

ACKNOWLEDGEMENTS

V. K. is thankful to UGC for the award of research fellowship. S.S.B. is a Women Scientist (DBT-BioCARe) receiving financial support from grant no GAP-2158. The work was supported by CSIR 12th FYP grant # BSC-0205.

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17 Plant material was collected between March and May (2013) from Forest Research Institute, New Forest Division, Deharadun (India). Plant was identified and authenticated at IIIM and herbarium sheet was prepared and submitted to Janaki Ammal herbarium, IIIM (Acronym RRLH, accession no. 22163). Dried samples of fruits were submitted to the institutional crude drug repository (accession no. 3893).

18 Isolation of chrotacumine K (**12**) and rohitukine (**1**) from fruits of *Dysoxylum binectariferum*: *D. binectariferum* fruits were air dried, seeds were removed and remaining parts were grinded to make coarse powder. The 90 g of fruits powder was extracted with methanol (250 ml x 3) for 2 hrs under continuous stirring. The solvent was evaporated under reduced pressure to get dried extract (3.26 g). The obtained extract was first dissolved in methanol (10 ml), followed by addition of chloroform (20 ml), which resulted in precipitation of polar constituents. White precipitate was filtered and and the filtrate obtained was subjected to silica gel column chromatography (n-Hexane-EtOAc). The column was charged with 100-200 mesh size silica gel and was eluted with increasing concentration of methanol in chloroform. At 7-8% of MeOH in chloroform, a new compound (non-polar to rohitukine) was eluted. The obtained compound was further purified by re-crystallization from chloroform to get cream colored solid (20 mg). At 12% MeOH in chloroform, a known alkaloid rohitukine (1) was isolated as yellow powder. Chrotacumine K (**12**): Creamish white solid; TLC: R_f = 0.67 (20% methanol-chloroform; HPLC purity: 98.8% (t_R =12.84 min); m.p. 194-196 °C; $[\alpha]^{20}_D$ = –13.46 (c 0.1, MeOH); ^{1}H NMR (400 MHz, $CDCl_3$): δ 12.86 (brs, 1H), 6.27 (s, 1H), 6.01 (s, 1H), 5.18 (brs, 1H), 3.57-3.52 (m, 1H), 3.22 – 3.12 (m, 3H), 2.49 (d, *J* = 12 Hz, 1H), 2.38 (s, 6H), 2.30 – 2.24 (s, 1H), 1.88 (s, 3H), 1.81 (d, *J* = 12 Mz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 182.76, 170.60, 166.35, 162.71, 160,79, 156.81, 108.13, 105.23, 104.43, 99.65, 71.14, 58.60, 56.19, 45.93, 35.71, 24.81, 21.01, 20.42; IR ($CHCl_3$): vmax 3584.10, 3352.59, 2923.01, 2852.49, 2346.36, 1736.94, 1660.76, 1614.91, 1588.33, 1419.56, 1389.74, 1260.17, 1189.03, 1020.38, 845.50, 759.15; ESI-MS: *m/z* 348.40 [M+H]+; HRMS: *m/z* 348.1453 calcd for $C_{18}H_{22}NO_6$+H^+ (348.1447). Rohitukine (**1**): yellow powder; TLC: R_f = 0.22 (20% methanol-chloroform); HPLC purity: > 99% (t_R = 11.13 min); mp. 215-218 °C; $[\alpha]^{20}_D$ = –17.07 (c 0.12, MeOH); ^{1}H NMR (400 MHz, CD_3OD): δ 6.15 (s, 1H), 5.97 (s, 1H), 4.14 (s, 1H), 3.62-3.59 (m, 1H), 3.49 (d, *J* = 8.4 Hz, 1H), 3.38 (t, *J* = 2, 4.4 Hz, 1H), 3.35 (d, *J* = 4 Hz, 1H), 3.22-3.20 (m, 1H), 3.15 (d, *J* = 12 Hz, 1H), 2.82 (s, 3H), 2.32 (s, 3H), 1.75 (d, *J* = 8 Hz, 1H); ^{13}C NMR (100 MHz, CD_3OD): δ 183.00, 167.70, 163.00, 160.70, 156.50, 107.40, 106.40, 104.00, 99.40, 66.70, 60.40, 55.40, 42.90, 35.70, 21.90, 18.90; IR ($CHCl_3$): ν_{max} 3584, 3312, 2956, 2920, 2870, 1741, 1653, 1460, 1378, 1248, 1082, 1020 cm^{-1}; ESI-MS: *m/z* 306.01 $[M+H]^+$; HRMS: *m/z* 306.1367 calcd for $C_{16}H_{20}NO_5$+H^+ (306.1341).

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Highlights

- A new chromone alkaloid chrotacumine K isolated**.**
- Schumaniofioside A reported for the first time from Meliaceae family.
- Biological evaluation of isolated compounds performed.
- Chrotacumine K showed potent inhibition of TNF-alpha and IL-6.
- Physichochemical properties were determined for bioactive compounds.

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