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Asperal: A New Clerodane Diterpene from *Sonchus asper*

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A new diterpenoid asperal (**1**) has been isolated from the chloroform soluble fraction of *Sonchus asper* along with two known compounds, emodin (**2**) and methyl-(3,8-di-hydroxy-6-methyl-9-oxo-9*H*-xanthene)-1-carboxylate (**3**) which were isolated for the first time from this species. The structures of the isolated compounds were assigned on the basis of ID and 2D NMR spectral analysis and by comparison with the reported data.

Keywords: *Sonchus asper*, Asteraceae, Clerodane diterpene.

INTRODUCTION

Sonchus asper (L.) Hill belongs to family Asteraceae andlocally named as Mahtari used in the treatment of liver injuries[1], protease inhibition and in the prevention of squamous cellcarcinoma of esophagus[2] as well as in human colorectal cancer[3]. This herb has also been credited in a variety of human disorder including wounds and burns[4] cough, bronchitis and asthma[5], gastrointestinal infection, inflammation, diabetes and cardiac dysfunction[6], kidney and liver disorders[7], reproductive disorder like impotence (erectile dysfunction) in humans[8], jaundice[9] and cancer[3]. Besides its pharmacological behavior, *S. asper* also contains secondary metabolites like flavonoids[10], terpenes and glycosides[11].

EXPERIMENTAL

The plant *Sonchus asper* was collected at Parachinar Kurram Agency, Khyber Pukhtunkhwa (N.W.F.P) Pakistan, in July, 2009 and was identified by a plant taxonomist. As the field from where the plant has been collected was open, no authority was responsible to issue permission and the study did not involve endangered and protected species. Likewise there was no restriction from land owner on usability of this specie and the permission was given from the land owner for the collection of this specie. After collection, the voucher specimen has been deposited in the herbarium of the Botany Department Kohat University of Science and Technology Kohat (KUST). The whole plant was air-dried for 10 days and milled into powder form with electrical grinder and finally stored in airtight bottles before subjecting to extraction process.

Extraction and isolation: The air-dried, ground whole parts of *Sonchus asper* (5 kg) were initially extracted with (12 L) MeOH at room temperature three times. The solvent was evaporated under reduced pressure to give a dark residue (130 g), which was partitioned between hexane (35 g), chloroform (55 g), butanol (15 g) and water (9 g). The chloroform extract was then subjected to silica gel chromatography using hexane with a gradient on chloroform up to 100 % and followed by methanol. Five fractions were collected. Fraction 1 (4.6 g) of the first column was loaded on silica gel and eluted with chloroform:hexane (8:2) to give compound **1** (10 mg). The compound **2** (8 mg) was isolated from chloroform soluble fraction eluted with chloroform:hexane (2.5:7.5) whereas the chloroform soluble fraction with chloroform:hexane (5:3) afforded compound **3** (25 mg), respectively.

General experimental procedures: UV and IR spectra were recorded on Hitachi-UV-3200 and Jasco-320-A spectrophotometers respectively. The ^{1}H and ^{13}C NMR and HMBC

spectra were recorded on Bruker spectrometers operating at 400 and 100 MHz, respectively, in CD_3OD using TMS as the internal standard. The chemical shift values are reported in ppm units and the coupling constants (*J*) are in Hz. EI-MS was recorded using JMS-HX-110 with a data acquisition system and on JMS-DA 500 mass spectrometers. The sample was subjected to column chromatography using silica gel (E. Merck, Darmstadt, Germany) having a 70-230 mesh size, followed by flash column chromatography using silica gel having a 230-400 mesh size. Thin layer chromatography was performed using pre-coated silica gel G-25-UV254 plates followed by UV light and by the ceric sulfate reagent and heating.

RESULTS AND DISCUSSION

The medicinal properties prompted us to carry out phytochemical investigation on *Sonchus asper*. Phytochemical investigation on title plant yield one new and two known compounds (Fig. 1). The chloroform soluble part obtained from the methanolic extract of *Sonchus asper* was subjected to silica gel column chromatography eluted with chloroform-hexane (8:2), resulted in a new clerodane type diterpeneasperal1 (Fig. 1). Compound **1** was obtained as an amorphous solid and its molecular formula was deduced as $C_{20}H_{28}O_4$ through EIMS. The $[M]^+$ peak at *m/z* 332.1817 in the HR-EI-MS, along with the examination of ^1H, ^{13}C NMR and DEPT spectra, showed a molecular formula of $C_{20}H_{28}O_4$, indicating six degrees of unsaturation and fragment ions at *m/z* 219, 201 and 173 showing diterpenoid skeleton having hydroxyl group and fragment ions at *m/z* 95, 81 and 67 confirming the presence of alkylated furan ring[12]. The functional groups were further supported by IR bands at 3470, 1510, 875 and 1750 cm^{-1} for hydroxyl group, furan ring and an aldehyde in the molecule, respectively.

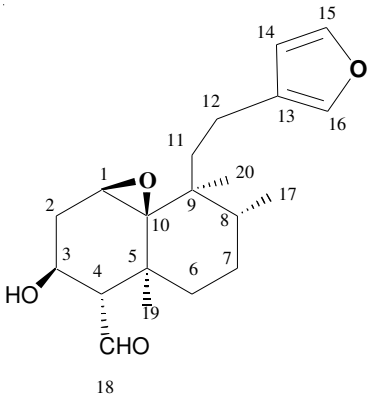


Fig.1. Chemical Structure of Asperal (**1**)

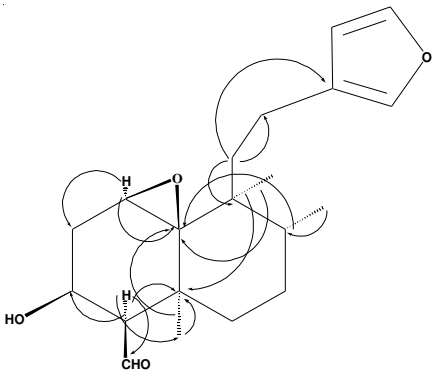
The ^1H NMR spectrum of **1** (Table-1) displayed three upfield signals, one for secondary methyl group at δ_H 0.90 (d, J = 7.3 Hz) and two for tertiary methyl groups at δ_H 1.00 and 1.23 (3H, s). A low field proton at δ_H 4.69 (t, J = 5.20 Hz) was attributed to C-1 having epoxide group. Another low field proton at δ_H 3.62 (dt, J = 3.2, 10.4, 13.7 Hz) was attributed to C-3 having hydroxyl moiety.

Typical high frequency signals at δ_H 6.22, 7.18 and 7.30 of three aromatic protons in the ^1H NMR spectrum of **1** were attributed to H-14, H-15 and H-16, respectively, suggesting the presence of furan ring[12,13]. The ^{13}C NMR spectrum (BB and DEPT, Table-1) of **1** corroborated the presence of three methyl, five methylenes, seven methines and five quaternary carbons. The upfield signals observed at δ_C 22.8, 22.1 and 16.4 were confirmed for three methyl groups at C-20, C-19 and C-17, respectively. These assessments divulge the *trans* pattern at the A/B ring junction of **1**[14]. A typical low field signals in ^{13}C NMR spectrum at δ_C 63.2 and 67.5 were inferred to C-1 and C-10 containing epoxy group.

TABLE-1
^1H AND ^{13}C NMR DATA (CD_3OD-400 MHz) OF COMPOUND **1**

Position	δ_H	δ_C
1	4.69 t (*J* = 5.20 Hz)	63.2
2	1.75 m	31.3
3	3.62 dt (*J* = 3.2, 10.4, 13.7 Hz)	78.2
4	2.19 d (*J* = 4.43 Hz)	34.7
5	-	43.7
6	1.75 m	18.0
7	1.75 m (overlapped)	18.1
8	2.05 m	39.2
9	-	43.4
10	-	67.5
11	1.79 t (*J* = 8.5 Hz)	20.7
12	2.06 t (8.5 Hz)	27.4
13	-	125.0
14	6.22 d (*J* = 1.8 Hz)	110.8
15	7.18 d (*J* = 1.8 Hz)	143.0
16	7.30 s	138.6
17	0.90 d (*J* = 6.13Hz)	23.4
18	-	178.1
19	1.23 s	22.6
20	1.00 s	21.8

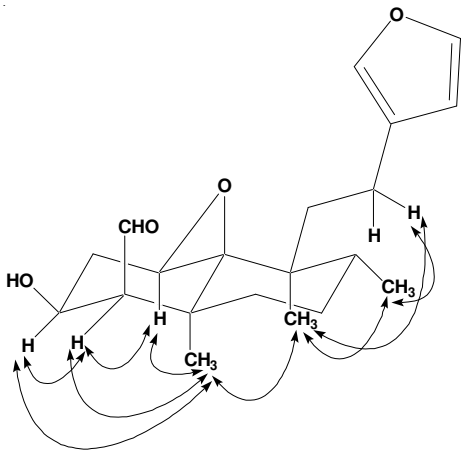
The HMBC (**Scheme-I**) of **1** revealed that the α-oriented CH_3-19 at δ_H 1.20 was correlated to the carbon atoms at δ_C 28.3 (C-4), 75.4 (C-6) and 32.2 (C-10), which established the presence of aldehyde moiety at C-4[15,16]. The signal in ^1H NMR at δ_H 1.50 could be assigned to CH_2-11, the HMBC of which showed correlations to the carbons at δ_C 32.2 (C-10), 39.3 (C-9), 44.8 (C-8), 22.9 (C-20) and 28.3 (C-12), confirming the attachment of the alkyl chain at C-9.



Scheme-I: Important HMBC correlations of Asperal **1**

The comparative stereochemistry of **1** was decided by judgment of the spectral data of **1** with those documented for other known diterpenoids[17] as well as from its NOESY spectrum (**Scheme-II**). The CH_3-19 displayed NOE relationship with H-1, H-3, H-4 and H-20, whereas CH_3-17 also demonstrated correlation with H-12 and H-20. This result is reliable with a *cis*-relationship between these groups and also symptomatic

of *trans*-fused A/B rings of decalin system of **1**. All chemical shift values were substantiated through ^{1}H NMR, ^{13}C NMR, HMBC and NOESY test and comparison with the reported data of related compounds[14]. From these interpretations and from the comparison of spectral data with the literature, the compound **1** determined to be commonly named asperal.



Scheme-II: Important NOESY correlations of Asperal **1**

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