Cyclopeptide Alkaloids of *Zizyphus* Species

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Summary: Cyclopeptide alkaloids isolated from the genus *Zizyphus* until 2000 have been reviewed and the distribution of individual compounds in various species have been discussed. Till now eighty one cyclopeptide alkaloids are reported from various *Zizyphus* species. This includes thirty five 13-membered, thirty nine 14-membered and seven 15-membered ring cyclopeptides in addition to one with open chain structure.

Introduction

Zizyphus is one of the important genus of the family *Rhamnaceae*. This *genus* comprises about 100 species distributed mostly in the tropical America, Africa, Mediterranean region, Indo-Malaya, Australia, Pakistan and India [1]. Only six species are indigenous to Pakistan viz: *Z. jujuba, Z. oxyphylla, Z. mauritiana, Z. nummularia, Z. rugosa* and *Z. spina-christi*. They are usually in the form of trees or shrubs, mostly armed with a pair of stipular spines [2].

Zizyphus species have tremendous uses in the folkloric/ Ayurvedic system of medicine. Fruits are used as laxative and expectorant. A wide spread remedy for almost any pain is a poultice of the powdered and backed roots while a root decoction is the accepted treatment among some Africans for tubercular gland swellings. Roots are also used by the sufferers of dysentery and lumbago [3]. The juice of the root bark is used as a purgative and externally used in rheumatism. Leaves are used for skin infections and tender leaves are used against scorpion sting while powdered bark is a domestic dressing to old wounds and ulcers [4]. Flowers together with leaves, are used in menorrhagia [5]. The stem bark is used to heal ulcers and wounds while the fruits are used in the treatment of bronchitis [6].

The root of *Z. lotus* is used as antidiabetic in traditional medicine while alkaloidal mixture of this species showed significant antibacterial activity [7].

The leaves of *Z. jujuba* have been reported to possess significant hypoglycemic activity when administered to diabetic rats [8]. It is also reported that the methanol extract of *Z. jujuba* have protective effect against the CCl_4-induced hepatotoxicity in rats [9]. Sanjoinine-A isolated from *Z. jujuba* is established to possess sedative activity which on heating changes to another isomer of greater activity [10,11]. It also showed strong prolongation activity on hexobarbitol induced sleeping time to mice [10]. Jujubosides A_1 and C and acetyljujuboside B, isolated from the seeds of *Z. jujuba*, were found to inhibit the histamine release from rat peritoneal exudate cells induced by antigen-antibody reaction [12].

The $CHCl_3$ and MeOH extracts of bark of *Z. spina-christi* showed antimicrobial activity against *E .coli, P. vulgaris, S. aureus, P.aeruginosa, C. albicans* and *B. subtilis* [13].

Since the previous reviews on cyclopeptide alkaloids by Warnhoff (1970) [14], Tschesche, *et al.*

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Table-1 :13, 14 and 15-Membered ring cyclopeptide alkaloids from the genus *Zizyphus*.

Comp. No.	Name (Mol. formula)	Physical data mp °C $[\alpha]_D$ (Mol. Weight)	Species	Part used	Ref.
	13-membered ring (Jubanine-A type)				
1.	Amphibine-H ($C_{33}H_{43}N_5O_6$)	205 [-570°(c:0.12, MeOH)] (607.7)	*Z.amphibia* *Z.spina-christi*	Stem bark Stem bark	18 19
2.	Daechucyclo-peptide-I ($C_{30}H_{38}N_4O_5$)	(534)	*Z.fructus*	Fruits	20
3.	Jubanine-A ($C_{40}H_{49}N_5O_6$)	105-110 [-326°] (695)	*Z.spina-christi* *Z.jujuba*	Stem bark Stem bark	19 21
4.	Jubanine-B ($C_{43}H_{47}N_5O_6$)	97-100 [-218°] (729)	*Z.jujuba*	Stem bark	21
5.	Jubanine-D ($C_{35}H_{47}N_5O_6$)	(617)	*Z.jujuba*	Root bark	22
6.	Lotusine-E ($C_{36}H_{49}N_5O_6$)	[-106°(c:1.0,$CHCl_3$)] (647)	*Z.lotus*	Root bark	7
7.	Lotusine-F ($C_{29}H_{36}N_4O_5$)	[-244°(c:0.5,$CHCl_3$)] (520)	*Z.lotus*	Root bark	7
8.	Mucronine-D ($C_{37}H_{51}N_5O_6$)	[-457°(c:1.0,$CHCl_3$)]	*Z.mucronata* *Z.nummularia*	Stem bark Root bark	23,24 25
9.	Transmucronine-D ($C_{28}H_{42}N_4O_5$)	153-154 [-418°(c:1.1,$CHlC_3$)] (514)	*Z.mucronata*	Roots	23
10.	O-Demethyl-mucronine-D ($C_{36}H_{49}N_5O_6$)	[-191°(c:0.3,$CHCl_3$)] (647)	*Z.mucronata*	Roots	23
11.	Nummularine-A ($C_{36}H_{49}N_5O_6$)	235-240 [-397°(c:0.2,$CHCl_3$)] (647.3683)	*Z.nummularia*	Root bark	25,26
12.	Nummularine-B ($C_{32}H_{41}N_5O_6$)	230-231 [-390°(c:0.2,$CHCl_3$)] (591.3)	*Z.nummularia* *Z.sativa*	Root bark Root bark	25,27,2 8 29
13.	Nummularine-C ($C_{31}H_{40}N_4O_5$)	278-280 [371°(c:0.2,$CHCl_3$)] (548.3002)	*Z.nummularia*	Root bark	25
14.	Nummularine-H ($C_{39}H_{47}N_5O_6$)	194-196 [-343(c:0.27,MeOH)] (681.3526)	*Z.nummularia*	Stem bark	30
15.	Nummularine-N ($C_{31}H_{41}N_5O_6$)	243-245 (591)	*Z.nummularia*	Stem bark	27
16.	Nummularine-P ($C_{29}H_{43}N_5O_6$)	143-144 (557.3213)	*Z.nummularia* *Z.rugosa*	Stem bark Stem bark	31 32
17.	Nummularine-R ($C_{33}H_{41}N_5O_5$)	134-135 ((587.3116)	*Z.nummularia*	Stem bark	33
18.	Nummularine-S ($C_{29}H_{36}N_4O_5$)	210-211 (520.2693)	*Z.nummularia*	Stem bark	34
19.	Nammularine-T ($C_{33}H_{41}N_5O_7$)	188-190 (619.2988)	*Z.nummularia*	Stem bark	35
20.	Rugosanine-A ($C_{30}H_{43}N_5O_7$)	237-240 (585.3177)	*Z.rugosa*	Stem bark	36
21.	Rugosanine-B ($C_{36}H_{39}N_5O_5$)	216-218 (621.3124)	*Z.rugosa*	Stem bark	32
22.	Sativanine-C ($C_{29}H_{43}N_5O_6$)	113-114 (557)	*Z.sativa*	Stem bark	37,38
23.	Sativanine-D ($C_{30}H_{43}N_5O_6$)	191-121 (569.3213)	*Z.sativa*	Stem bark	39
24.	Sativanine-E ($C_{33}H_{41}N_5O_5$)	127-128 [-99°(c:0.2,$CHCl_3$)] (587.3114)	*Z.sativa*	Stem bark	40
25.	Sativanine-F ($C_{34}H_{43}N_5O_7$)	139-141 (633.3164)	*Z.sativa*	Root bark	41

Table-1 : (Continued)

Comp. No.	Name (Mol. formula)	Physical data mp °C $[\alpha]_D$ (Mol. Weight)	Species	Part used	Ref.
26.	Sativanine-G ($C_{28}H_{42}N_4O_5$)	92 (514.3168)	*Z.sativa*	Stem bark	42
27.	Sativanine-H ($C_{29}H_{43}N_5O_6$)	191-192 (557.3213)	*Z.sativa* *Z.rugosa*	Stem bark Stem bark	38 32
28.	Sativanine-K ($C_{27}H_{38}N_4O_6$)	160-162 (514.2778)	*Z.sativa*	Stem bark	43
29.	Tscheschamine ($C_{29}H_{36}N_4O_5$)	197-198 (520.2688)	*Z.sativa*	Stem bark	44
13-Membered ring (Zizyphine-A type)					
30.	Zizyphine-I ($C_{36}H_{47}N_5O_6$)	(645)	*Z.oenoplia*	Stem bark	45
31.	Zizyphine-A ($C_{33}H_{49}N_5O_6$)	124-126 [+411°(c:0.086, $CHCl_3$)] (611)	*Z.oenoplia*	Stem bark	15,46 47,48
32.	Zizyphine-B ($C_{32}H_{47}N_5O_6$) [N-Acetyl of ($C_{34}H_{49}N_5O_7$)]	(597) N-Acetyl of: [-383±6°(c:0.1,$CHCl_3$) (639.3632)]	*Z.oenoplia*	Stem bark	15
33.	Zizyphine-C ($C_{36}H_{47}N_5O_6$)	[-331±5°(c:0.1,$CHCl_3$)] (645.3526)	*Z.oenoplia*	Stem bark	15
34.	Zizyphine-F ($C_{32}H_{47}N_5O_6$)	235 [-277°(c:0.15,MeOH)] (597)	*Z.oenoplia* *Z.spina-christi*	Stem bark Stem bark	49 19
35.	Hysodricanine-B ($C_{30}H_{43}N_5O_6$)	35 (569)	*Z.hysodrica*	Leaves	50
14-Membered ring (Frangulanine type)					
36.	Amphibine-A ($C_{33}H_{43}N_5O_4$)	237-239 [-310°(c:0.021, MeOH)] (573)	*Z.amphibia*	Stem bark	51
37.	Scutianine-C ($C_{32}H_{33}N_3O_5$)	323-334 [-188°(c:0.15,$CHCl_3$)] (539)	*Z.nummularia* *Scutia buxifolia*	Stem bark Roots	35 52
38.	Frangufoline ($C_{31}H_{42}N_4O_4$)	244 [-299°(c:0.1,$CHCl_3$)] (534)	*Z.jujuba* *Z.nummularia* *Z.lotus* *Z.vulgaris*	Stem bark Stem bark Aerial seeds	33,53 54 55 56
39.	Franganine ($C_{28}H_{44}N_4O_4$)	(500)	*Z.spina-christi*	Stem bark	13
40.	Lotusanine-A ($C_{31}H_{42}N_4O_4$)	Amorphous (534)	*Z.lotus*	Aerial	55
41.	Lotusanine-B ($C_{37}H_{40}N_4O_5$)	Amorphous (620.2999)	*Z.lotus*	Aerial	55
42.	Nummularine-D ($C_{30}H_{40}N_4O_4$)	265-268 [-186°(c:0.2,$CHCl_3$)] (520.3050)	*Z.nummularia*	Root bark	26
43.	Nummularine-E ($C_{29}H_{38}N_4O_4$)	278-279 [+12°(c:0.02,MeOH)] (522.2824)	*Z.nummularia*	Root bark Stem bark	45 57
44.	Nummularine-G ($C_{31}H_{40}N_4O_4$)	174-175 [-133°(c:0.085,MeOH)] (532.3050)	*Z.nummularia*	Stem bark	30
45.	Nummularine-K ($C_{33}H_{43}N_5O_4$)	237-239 [-45°(c:0.04, MeOH)] (573.3315)	*Z.nummularia* *Z.xylopora*	Stem bark Stem bark	30 33
46.	Nummularine-M ($C_{31}H_{42}N_4O_4$)	263-265 [-46.66°(c:0.1,$CHCl_3$)] (534.3174)	*Z.nummularia*	Stem bark	27

Table-1 : (continued)

Comp. No.	Name (Mol. formula)	Physical data mp °C $[\alpha]_D$ (Mol. Weight)	Species	Part used	Ref.
47.	Sanjoinenine ($C_{29}H_{35}N_3O_4$)	281-282 [-272.5(c:1.6,Pyridine)] (489.2627)	*Z.vulgaris* *Z.lotus* *Z.spinosa-semen*	Seeds Aerial Stem bark	56 55 10
48.	Sanjoinine-A ($C_{31}H_{42}N_4O_4$)	(534)	*Z.spinosa-semen* *Z.jujuba*	Stem bark Fruits	10 11
49.	Sanjoinine-B ($C_{30}H_{40}N_4O_4$)	212-214 (520)	*Z.spinosa-semen* *Z.vulgaris*	Stem bark Seeds	10 56
50.	Sanjoinine-F ($C_{31}H_{42}N_4O_5$)	228-229 [-107°(0.05,$CHCl_3$)] (550)	*Z.lotus* *Z.vulgaris*	Aerial Seeds	55 56
51.	Sativanine-A ($C_{30}H_{40}N_4O_4$)	80 (520.3050)	*Z.sativa* *Z.spina-christi*	Stem bark Stem bark	29 13
52.	Sativanine-B ($C_{30}H_{38}N_4O_4$)	Amorphous (518.2893)	*Z.sativa*	Stem bark	29
14-Membered ring (Amphibine-B type)					
53.	Amphibine-B ($C_{39}H_{47}N_5O_5$)	[-181°(c:0.08,MeOH)] (665.3577)	*Z.amphibia*	Stem bark	58
54.	Amphibine-C ($C_{36}H_{49}N_5O_5$)	[-224°(c:0.075,MeOH)] (631.3734)	*Z.amphibia*	Stem bark	58
55.	Amphibine-D ($C_{36}H_{49}N_5O_5$)	[-203°(c:0.09,MeOH)] (631.3734)	*Z.amphibia* *Z.vulgaris*	Stem bark Seeds	58 56
56.	Amphibine-E ($C_{38}H_{50}N_6O_5$)	[-175°(c:0.14, MeoH)] (670.3843)	*Z.amphibia*	Stem bark	58
57.	Amphibine-F ($C_{29}H_{36}N_4O_4$)	Amorphous [-171°(c:0.26,$CHCl_3$)] (504.2737)	*Z.amphibia*	Stem bark	18
58.	Amphibine-G ($C_{32}H_{39}N_5O_4$)	182-185 [-218°(c:0.24,$CHCl_3$)] (557.3002)	*Z.amphibia*	Stem bark	18
59.	Hysodricanine-A ($C_{35}H_{45}N_5O_5$)	93-96 [-215°] (615)	*Z.hysodrica*	Leaves	59
60.	Lotusine-A ($C_{30}H_{38}N_4O_4$)	[-215°(c:1.0,$CHCl_3$)] (518)	*Z.lotus*	Root bark	60
61.	Lotusine-B ($C_{36}H_{49}N_5O_5$)	[-179°(c:0.32, $CHCl_3$)] (631)	*Z.lotus*	Root bark	7
62.	Lotusine-C ($C_{35}H_{47}N_5O_5$)	[-168°(c:0.5,$CHCl_3$)] (617)	*Z.lotus*	Root bark	7
63.	Lotusine-D ($C_{29}H_{36}N_4O_4$)	[187°(c:0.5,$CHCl_3$)] (504)	*Z.lotus*	Root bark	60
64.	Mauritine-A ($C_{32}H_{41}N_5O_5$)	104 [-315°(c:0.33,MeOH)] (575)	*Z.mauritiana* *Z.spina-christi*	Stem bark Stem bark	61 62
65.	Mauritine-B ($C_{35}H_{47}N_5O_5$)	[-151°(c:0.44,MeOH)] (617)	*Z.mauritiana*	Stem bark	61
66.	Mauritine-C ($C_{29}H_{36}N_4O_4$)	(504)	*Z.spina-christi*	Stem bark	13
67.	Mauritine-H ($C_{33}H_{43}N_5O_5$)	212-215 [-169°] (589)	*Z.mauritiana*	Stem bark	59
68.	Mucronine-J ($C_{27}H_{41}N_4O_4$)	Amorphous [-236°(c:1.0,$CHCl_3$)] (485)	*Z.mucronata*	Root bark	63
69.	Nummularine-F ($C_{33}H_{32}N_4O_4$)	120 [-204(c:0.2,MeOH)] (428.2424)	*Z.nummularia*	Root bark	26
70.	Zizyphine-H ($C_{28}H_{34}N_4O_4$)	150 (490)	*Z.oenoplia*	Stem bark	46

Table-1 : (continued)

Comp. No.	Name (Mol. formula)	Physical data mp °C $[\alpha]_D$ (Mol. Weight)	Species	Part used	Ref.
14-Membered ring (Zizyphine-G type)					
71.	Sanjoine-D ($C_{24}H_{32}N_4O_4$)	175-176 [-121°(c:0.1,MeOH)] (440.2418)	*Z.nummularia*	Stem bark	43
72.	Zizyphine-G ($C_{24}H_{32}N_4O_4$)	130 [-185°(c:0.19, MeOH)] (440)	*Z.oenoplia*	Stem bark	19,49
14-Membered ring (Sanjoinine-D type)					
73.	Sanjoinine-D ($C_{32}H_{46}N_4O_5$)	256-258 [-53.6(c:0.25,$CHCl_3$)] (566.3468)	*Z.vulgaris* *(Z.spinosus-semen)*	Seeds	10,56
74.	Sanjoinine-G1 ($C_{31}H_{44}N_4O_5$)	(552)	*Z.vulgaris*	Seeds	17
15-Membered ring (Mucronine-A type)					
75.	Abyssinine-A ($C_{25}H_{38}N_4O_4$)	(458)	*Z.oenoplia*	Stem bark	15,46
76.	Abyssinine-B ($C_{25}H_{38}N_4O_4$)	(458)	*Z.oenoplia*	Stem bark	15,50
77.	Mucronine-A ($C_{28}H_{36}N_4O_4$)	(492)	*Z.mucronata*	Stem bark	24,64
78.	Mucronine-B ($C_{27}H_{34}N_4O_4$)	(478)	*Z.mucronata*	Stem bark	24,64
79.	Mucronine-C ($C_{25}H_{38}N_4O_4$)	(458)	*Z.mucronata*	Stem bark	24,64
80.	Zizyphine-D ($C_{25}H_{38}N_4O_5$)	195-196 [+236±4°(c:0.1,$CHCl_3$)] (474.2842)	*Z.oenoplia*	Stem bark	15
81.	Zizyphine-E ($C_{24}H_{36}N_4O_5$)	Amorphous [+150±2°(c:0.1,$CHCl_3$)] (460.2686)	*Z.oenoplia*	Stem bark	15
82.	Sanjoinine-G2 ($C_{30}H_{42}N_4O_5$)	182 [-79.2(c:0.275,$CHCl_3$)] (538.3155)	*Z.vulgaris*	Seeds	56

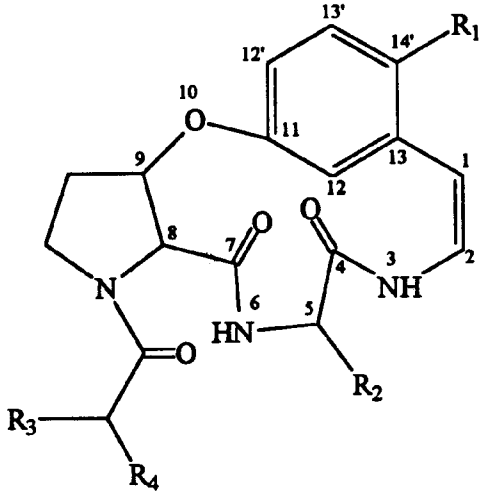
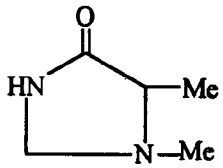


Table-2 : Structures of 13-membered ring cyclopeptide alkaloids.

Str. No.	R1	R2	R3	R4
1.	OMe	CH_2CHMe_2	CH_2-Indolyl	NMe_2
2.	OH	$CH(Me)CH_2Me$	CH_2Ph	NMe_2
3.	OMe	$CH(Me)CH_2Me$	CH_2Ph	$NH.CO.CH(NMe_2)CH_2Ph$
4.	OMe	CH_2Ph	CH_2Ph	$NH.CO.CH(NMe_2)CH_2Ph$
5.	H	$CH(Me)CH_2Me$	$CHMe_2$	$NH.CO.CH(NMe_2)NMe_2$
6.	OH	$CH(Me)CH_2Me$	CH_2Ph	$NH.CO.CH(NMe_2)CH_2CHMe_2$
7.	OH	$CH(Me)CH_2Me$	CH_2Ph	NHMe
8.	OMe	$CH(Me)CH_2Me$	CH_2CHMe_2	$NH.CO.CH(NMe_2)CH_2Ph$
9.	OMe	$CH(Me)CH_2Me$	CH_2CHMe_2	NMe_2
10.	OH	$CH(Me)CH_2Me$	CH_2CHMe_2	$NH.CO.CH(NMe_2)CH_2Ph$
11.	OMe	$CH(Me)CH_2Me$	CH_2CHMe_2	$NH.CO.CH(NHMe)CH_2Ph$
12.	OMe	CH_2Ph	$CHMe_2$	$NH.CO.CH(NHMe)Me$
13.	OMe	CH_2CHMe_2	CH_2Ph	NMe_2
14.	OMe	CH_2Ph	CH_2Ph	$NH.CO.CH(NHMe)CH_2Ph$
15.	OMe	CH_2Ph	$CHMe_2$	$NH.CO.CH_2NMe_2$
16.	OMe	CH_2CHMe_2	$CHMe_2$	$HN.CO.CH(NHMe)Me$
17.	OMe	$CH(Me)CH_2Me$	CH_2-Indolyl	NMe_2
18.	OMe	CH_2Ph	$CHMe_2$	NH_2
19.	OMe	CH_2Ph	$CHMe_2$	$NH.CO.CH(Me)N(Me)CHO$
20.	OMe	CH_2CHMe_2	$CHMe_2$	$NH.CO.CH(Me)N(Me)CHO$
21.	OMe	CH_2Ph	CH_2-Indolyl	NMe_2
22.	OMe	$CH(Me)CH_2Me$	$CHMe_2$	$CH(Me)NHMe$
23.	OMe	$CH(Me)CH_2Me$	$CHMe_2$	
24.	OMe	CH_2CHMe_2	CH_2-Indolyl	NMe_2
25.	OMe	CH_2Ph	$CHMe_2$	$NH.CO.CH(NHCHO)CHMe_2$
26.	OMe	$CH(Me)CH_2Me$	$CH(Me)CH_2Me$	NMe_2
27.	OMe	CH_2CHMe_2	$CHMe_2$	$NH.CO.CH_2NMe_2$
28.	OMe	$CH(Me)CH_2Me$	$CH(Me)CH_2Me$	NHCHO
29.	OMe	CH_2Ph	$CH(Me)CH_2Me$	NH_2

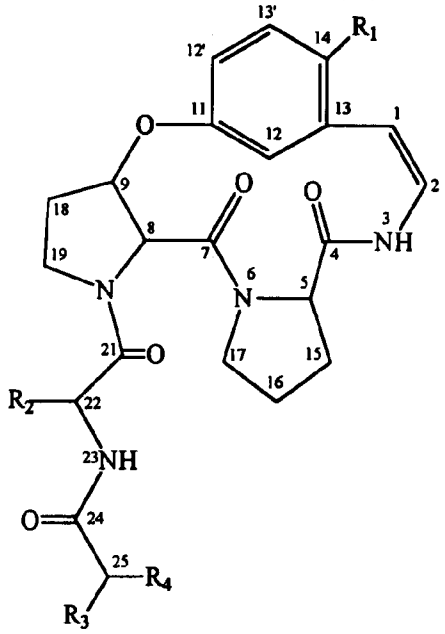


Table-2 : (continued).

Str. No.	R1	R2	R3	R4
30.	OMe	CH_2Ph	NMe_2	$CH(Me)CH_2Me$
31.	OMe	$CH(Me)CH_2Me$	NMe_2	$CH(Me)CH_2Me$
32.	OMe	$CH(Me)CH_2Me$	NHMe	$CH(Me)CH_2Me$
33.	OMe	$CH(Me)CH_2Me$	NMe_2	Ph
34.	OH	$CH(Me)CH_2Me$	Me	$CH(Me)CH_2Me$
35.	H	$CH(Me)CH_2Me$	NMe_2	Me

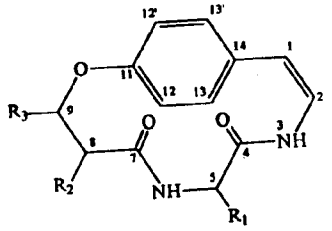
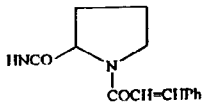
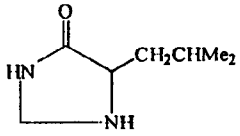
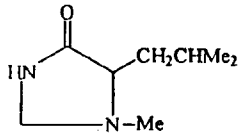
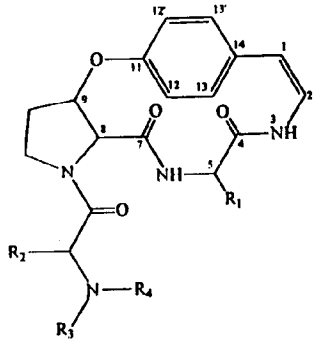
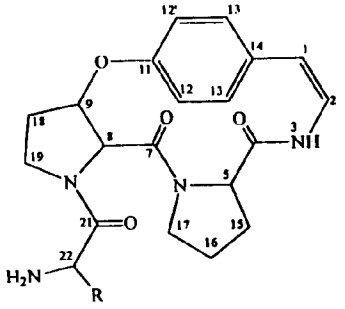


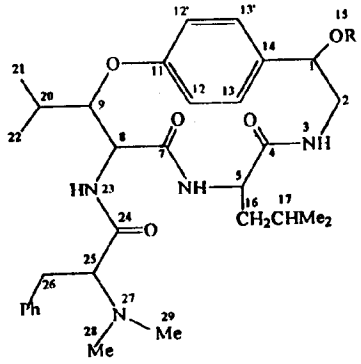
Table-3 : Structures of 14-membered ring Cyclopeptide Alkaloids.

Str. No.	R1	R2	R3
36.	$CH(Me)CH_2Me$	NH.CO.CH(NMe_2)CH_2-Indolyl	$CHMe_2$
37.	CH(OH)Ph	NH.CO.CH:CHPh	$CHMe_2$
38.	CH_2CHMe_2	NH.CO.CH(NMe_2)CH_2Ph	$CHMe_2$
39.	CH_2CHMe_2	NH.CO.CH(NMe_2)CH_2CHMe_2	$CHMe_2$
40.	$CH(Me)CH_2Me$	NH.CO.CH(NMe_2)CH_2Ph	$CHMe_2$
41.	CH_2Ph		$CHMe_2$
42.	CH_2CHMe_2	NH.CO.CH(NHMe)CH(Me)CH_2Me	Ph
43.	CH_2CHMe_2	NH.CO.CH(NMe_2)CH(OH)Me	Ph
44.	CH_2CHMe_2		Ph
45.	CH_2CHMe_2	NH.CO.CH(NMe_2)CH_2-Indolyl	$CHMe_2$
46.	CH_2CHMe_2	NH.CO.CH(NMe_2)CH(Me)CH_2Me	$CHMe_2$
47.	CH_2CHMe_2	NH.CO.CH:CHPh	$CHMe_2$
48.	CH_2CHMe_2	NH.CO.CH(NMe_2)CH_2Ph	$CHMe_2$
49.	CH_2CHMe_2	NH.CO.CH(NHMe)CH_2Ph	$CHMe_2$
50.	$CH(OH)CHMe_2$	NH.CO.CH(NMe_2)CH_2Ph	Ph
51.	CH_2CHMe_2	NH.CO.CH(NMe_2)CH(Me)CH_2Me	Ph
52.	$CHMe_2$		



Str. No.	R1	R2	R3	R4
53.	CH_2Ph	$CH(Me)CH_2Me$	H	$CO.CH(NMe_2)CH_2Ph$
54.	CH_2Ph	$CH(Me)CH_2Me$	H	$CO.CH(NMe_2)CH_2CHMe_2$
55.	$CH(Me)CH_2Me$	$CH(Me)CH_2Me$	H	$CO.CH(NMe_2)CH_2Ph$
56.	$CH(Me)CH_2Me$	CH_2-Indolyl	H	$CO.CH(NMe_2)CH_2Ph$
57.	CH_2Ph	$CH(Me)CH_2Me$	H	Me
58.	CH_2CHMe_2	CH_2-Indolyl	Me	Me
59.	$CH(Me)CH_2Me$	CH_2Ph	H	$CO.CH(NMe_2)CH_2CHMe_2$
60.	$CH(Me)CH_2Me$	CH_2Ph	Me	Me
61.	$CH(Me)CH_2Me$	CH_2Ph	H	$CO.CH(NMe_2)CH_2CHMe_2$
62.	$CH(Me)CH_2Me$	CH_2Ph	Me	$CO.CH(NHMe)CHMe_2$
63.	$CH(Me)CH_2Me$	CH_2Ph	H	Me
64.	CH_2Ph	$CHMe_2$	H	$CO.CH.(NMe_2)Me$
65.	CH_2Ph	$CHMe_2$	H	$CO.CH(NMe_2)CH(Me)CH_2Me$
66.	CH_2Ph	$CH(Me)CH_2Me$	H	Me
67.	CH_2Ph	$CH(Me)CH_2Me$	H	$CO.CH(NMe_2)CH_2(Me)CH_2Me$
68.	$CH(Me)CH_2Me$	CH_2CHMe_2	Me	Me
69.	$CH(Me)CH_2Me$	H	Me	Me
70.	CH_2Ph	$CH(Me)CH_2Me$	H	H





Str. #	R
71.	CH_2CHMe_2
72.	$CH(Me)CH_2Me$
73	R= Me
74	R=H

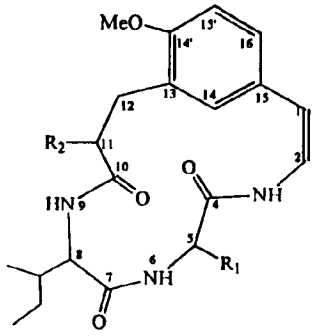


Table-4 : Structures of 15-membered ring Cyclopeptide Alkaloids.

Str. #	R1	R2
75.	CH_2CHMe_2	NHMe
76.	$CH(Me)CH_2Me$	NHMe
77.	CH_2Ph	NMe_2
78.	CH_2Ph	NHMe
79.	CH_2CHMe_2	NMe_2
80.	$C(Me)(OH)CH_2Me$	NHMe
81.	$C(Me)(OH)CH_2Me$	NH_2

(1974) [15] and Shah *et al.* (1985) [16] many new compounds have been isolated and their structures established. The purpose of the present review is to tabulate the cyclopeptide alkaloids obtained from the genus *Zizyphus* along with their structures and physical data. This will provide an easy reference source for alkaloids isolated from various *Zizyphus* species.

The genus *Zizyphus* is very popular for its cyclopeptide alkaloids. There are more than 81 such alkaloids isolated from different *Zizyphus* species that includes 13, 14 & 15 - membered ring systems (Table 1). The classification of this group of natural products has been adopted on the basis of the size of the ring [16].

The 13-membered cyclopeptide alkaloids include 29 jubanine-A type (**1-29**) and 6 zizyphine-A type (**30-35**) compounds. The basic unit of these alkaloids is formed from bounding of 2-methoxy-5-hydroxy styrylamine unit to an α-amino acid and α, β-hydroxy-α-amino acid forming a ring.

The alkaloids of 14-membered rings include 17 frangulanine-B type (**36-52**), 18 amphibine-B type (**53-70**), 2 zizyphine-G type (**71-72**) and 2 sanjoinine-D type (**73-74**) cyclopeptide alkaloids. The basic skeleton of the ring consist of β-hydroxy styryl amine, α-amino acid and β-hydroxy-α-amino acid. Sanjoinine-D (**73**) and sanjoinine-G1 isolated from *Z. spinosus-semen* [10] and *Z. vulgaris* [17] are the only cyclopeptide alkaloids with methoxyl and hydroxyl groups at C-1 of styrylamine moiety, respectively, instead of usual carbon-carbon double bond.

The 15-membered ring cyclopeptide alkaloids isolated from *Zizyphus* species are 7 in number. The ring of this macro cyclic system is composed of 5-(N-methyl or N, N-dimethyl alaninyl)-4-methoxy-α-styrylamine unit and two amino acids (leucine, isoleucine or phenyl alanine). The ring is closed by direct substitution of the aromatic nucleus of the styryl amine by an amino acid instead of usual ether linkage (**75-81**).

The plants containing these alkaloids, have a wide range of folkloric activities but, with the exception of few, none of them can reasonably be attributed to the peptide alkaloids as yet. This might be due to inadequate quantities of material available for pharmacological testing. Hopefully these alkaloids will be subjected to more general screening in the near future.

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