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Crassulaceae (chemistry and pharmacology) - A review

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ABSTRACT

Family Crassulaceae comprises approximately 1410 species which are commonly used for ornamental purposes. And nowadays showed many medicinal values. Recently, it has had been reported that several species of the family possess certain biological and pharmacological activities as: anti-oxidant, anti-hyperglycemic, antimicrobial, antiulcerogenic, cytotoxic/anti-cancer, anti-inflammatory, anti-nociceptive activity, hepatoprotective, analgesic, anti-arthritic, anti-malarial, antimutagenic, insecticidal, anti-thrombolytic, antihypertensive and myometrial activities. Earlier studies on different Crassulaceae plants have reported the isolation of flavonoids, sterols, ascorbic acid, trace elements, organic acids, hydrocarbons, triterpenoids, phenolic components and bufadienolides. This review contains an overview on the chemistry and pharmacological activities of Family Crassulaceae.

1. Introduction

Species of family Crassulaceae (stonecrop family) are very diverse ranging from tiny insignificant annual herbs to perennial shrubs and trees. Many of the species have attractive flowers. The entire family consists of 35 genera and 23 hybrid genera with a total of 1410 species and 305 intraspecific taxa [1].

The largest genus is *Sedum* (stonecrop, wall pepper) with 428 species. Other large genera are *Aeonium* (36 species), *Crassula* (195 species), *Dudleya* (47 species), *Echeveria* (139 species), *Kalanchoe* (144 species), *Rhodiola* (58 species), Sempervivum (63 species), and *Tylecodon* (46 species). These are commonly used as ornamental plants [2].

The phytochemical studies showed that most plants belonging to this family contain 55 different types of phenolic compounds, eight steroidal compounds and eight bufadienolides and cardenolides isolated from family Crassulaceae.

The pharmacological studies showed many biological activities like anti-oxidant, antihyperglycemic, antimicrobial, antiulcerogenic, cytotoxic/anti-cancer, anti-inflammatory & anti-nociceptive activity, hepatoprotective, analgesic, anti-arthritic, anti-malarial, anti-mutagenic, insecticidal, anti-thrombolytic, antihypertensive and myometrial activities. Table 1.

2. Phytochemical constituents

2.1. Phenolic compounds (Table 1)

Family Crassulaceae is a rich source of phenolic compounds. Reviewing the current literature, it was reported that the major flavonoids and phenolic compounds such as Kaempferol (1) was isolated from *Crassula capitella* [3], *Jovibarba sobolifera* [4], *Orostachys japonicas* [5], *Rhodiola sachalinensis* [6], *Kalanchoe spathulata* [7], *K. gracilis* [7] and *Bryophyllum pinnatum* [8], Quercetin (2) was isolated from *C. capitella* [3], *Kalanchoe beharensis* [9], *K. longiflora* [9], *B. pinnatum* [8], *J. sobolifera* [4], *K. spathulata* [7], *K. gracilis* [7], *K. blossfeldiana* [7], *K. marmorata* [7] and *O. japonicas* [5], Apigenin (3), Apigetrin (4) and Apiin (5) isolated from *Sedum caeruleum*. [10], Astragallin 6″-gallate (6), Ethyl 3,5 dihydroxy 4-methoxy benzoate (7), Ethyl gallate (8), Gallic acid (9), Methyl gallate (10) and bergenin (11) isolated from *C. capitella* [3], Rhodionin (12), Rhodiosin (13), kaempferol-3, 4′-di-*O*-β-D-glucopyranoside (14), Multiflorin B (15) and salidroside (16) isolated from *Rhodiola sachalinensis* [6] and from *Rhodiola crenulata* [11], Afzelin (17) isolated from *Rhodiola sachalinensis* [6], *Bryophyllum pinnatum* [7] and from *Rhodiola crenulata* [11], kaempferol 3,7,4′-*O*-trimethylether (18),kaempferol-3-*O*-α-L-rhamnopyranosyl-7-*O*-α-D-glucofuranosyl-(1 → 2)-*O*-α-L-rhamnopyranoside (19), kaempferol 3-*O*-β-D-glucopyranoside-7-*O*-α-L-rhamnopyranoside (20), kaempferol 3-*O*-β-D-glucoside (21) and

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Table 1
Phenolic compounds isolated from family Crassulaceae.

Compound	Compound number	Species	Ref.
α-rhamnoisorobin	**80**	*Bryophyllum pinnatum*	[7]
2-(4-hydroxyphenyl)-ethyl-*O*-β-D-gluco-pyranosyl-6-*O*- β -D-glucopyranoside	**39**	*Rhodiola crenulata*	[11]
3′,4′-dimethoxy quercetin	**81**	*K. pinnata*	[7]
4′-*O*-β-D-glucopyranosyl-cis-*p*-coumaric acid	**31**	*Bryophyllum pinnatum*	[8]
4‴'-acetylsagittatin A	**68**	*K. streptantha*	[7]
8-methoxyquercetin-3,7-di-*O*- rhamnopyranoside	**71**	*K. brasiliensis*	[7]
8-methoxykaempferol-3,7-di-*O*- rhamnopyranoside	**72**	*K. pinnata* *K. gastonisbornieri*	
11-*O*-(4′-*O*-methyl galloyl)-bergenin	**23**	*Crassula capitella*	[3]
11-*O*-galloyl bergenin	**27**	*Crassula capitella*	[3]
4-methoxy-3, 5 dihydroxy methyl benzoate	**24**	*Crassula capitella*	[3]
Acacetin-7-*O*-α-L-rhamnopyranosyl-(1 → 6)-β-D-glucopyranoside	**32**	*Bryophyllum pinnatum*	[8]
Afzelin	**17**	*Rhodiola sachalinensis.* *Bryophyllum pinnatum* *Rhodiola crenulata*	[6,7] [8,11]
Apigenin	**3**	*Sedum caeruleum.*	[10]
Apigenin-6-C-β-D-glucopyranosyl-8-C-β-D-glucopyranosyl (vicenin-2)	**30**	*Kalanchoe gastonis*	[13]
Apigetrin	**4**	*Sedum caeruleum.*	[10]
Apiin	**5**	*Sedum caeruleum.*	[10]
Astragallin 6″-gallate	**6**	*Crassula capitella*	[3]
Bergenin	**11**	*Crassula capitella*	[3]
Diosmetin 7-*O*-α-L-rhamnopyranosyl-(1 → 6)-β-D-glucopyranoside	**33**	*Bryophyllum pinnatum*	[8]
Ethyl 3,5 dihydroxy 4-methoxy benzoate	**7**	*Crassula capitella*	[3]
Ethyl gallate	**8**		
Eupafolin	**63**	*K. gracilis*	[7]
Eupafolin-4′-*O*-rhamnoside	**58**		
Eupafolin-3-7 di-*O*-rhamnoside	**59**		
Eupafolin-3-*O*-rhamnosyl-7-*O*-(4-*O*- acetylrhamnoside)	**60**		
Eupafolin-3-*O*-(3-*O*acetylrhamnosyl)-7-*O*-(3-*O*acetylrhamnoside)	**61**		
Gallic acid	**9**	*Crassula capitella*	[3]
Herbacetin-3-*O*-β-D-gluco-pyranosyl-7-*O*-α-L-rhamnopyranoside	**44**	*Rhodiola rosea*	[12]
Herbacetin-8-*O*-β-D-glucopyranoside	**45**	*Rhodiola rosea*	[12]
Icariside D2	**40**	*Rhodiola crenulata*	[11]
Isorhamnetin-3-O-α-L-1C4-rhamnopyranoside, 4′-methoxy-myricetin-3-O-α-L-1C4-rhamnopyranoside	**73**	*K. marmorata*	[7]
Kaempferitrin	**75**	*K. pinnata*	[7]
Kaempferol	**1**	*Crassula capitella,* *Jovibarba sobolifera.* *Orostachys japonicas,* *Rhodiola sachalinensis.* *Bryophyllum pinnatum*	[3–6,8]
Kaempferol 3,7,4′-*O*-trimethylether	**18**	*Jovibarba sobolifera.*	[4]
Kaempferol 3-*O*-galactopyranosy1-(1 → 2)-*O*-α-L-rhamnopyranoside	**22**	*Jovibarba sobolifera.*	[4]
Kaempferol 3-*O*-α-D-arabinopyranoside	**25**	*Crassula capitella*	[3]
Kaempferol 3-*O*-α-L-arabinopyranosyl-(1 → 2)-α-L-rhamnopyranoside	**34**	*Bryophyllum pinnatum*	[8]
Kaempferol-3-*O*-rhamnoside	**57**	*K. spathulata*	[7]
Kaempferol 3-*O*-α-L-rhamnopyranosyl-7-*O*-α-D-glucofuranosyl-(1 → 2)-*O*-α-L-rhamnopyranoside	**19**	*Jovibarba sobolifera.*	[4]
Kaempferol 3-*O*-β-D-glucopyranoside-7-*O*-α-L-rhamnopyranoside	**20**	*Jovibarba sobolifera.* *Rhodiola rosea*	[4] [12]
Kaempferol 3-*O*-β-D-glucoside	**21**	*Jovibarba sobolifera.*	[4]
Kaempferol 3-rutinoside	**47**	*Orostachys japonicas*	[5]
Kaempferol-3, 4′-di-*O*-β-D-glucopyranoside	**14**	*Rhodiola sachalinensis.*	[6]
Kaempferol-3, 7-di-*O*-glucoside	**49**	*O.margaritifolius*	[5]
Kaempferol-3-*O*-β-D-glucopyranoside-(2 → 1)-β-D-xylopyranoside	**46**	*Rhodiola rosea*	[12]
Kaempferol-3-rhamnosyl-7-glucoside	**50**	*O.margaritifolius*	[5]
Kampferol-3,7-di-*O*-α-L-rhamnopyranoside	**53**	*Kalanchoe beharensis and K. longiflora.*	[9]
Kampferol-3-*O*-α-L-rhamnopyranoside	**55**	*Kalanchoe beharensis and K. longiflora.*	[9]
Kaempferol 3-*O*-α-L-(2-acetyl)rhamnopyranoside-7-O-α-L-rhamnopyranoside	**76**	*Bryophyllum pinnatum*	[7]
Kaempferol 3-*O*-α-L-(3-acetyl)rhamnopyranoside-7-O-α-L-rhamnopyranoside	**77**		
Kaempferol 3-*O*-α-L-(4-acetyl)rhamnopyranoside-7-O-α-L-rhamnopyranoside	**78**		
Kaempferol 3-*O*-α-L-(4-acetyl)rhamnopyranoside-7-O-α-L-rhamnopyranoside	**79**		
Kapinnatoside	**69**	*K. pinnata*	[7]
Luteolin	**62**	*K. gracilis*	[7]
Methyl gallate	10	*C. capitella*	[3]
Multiflorin B	**15**	*Rhodiola sachalinensis* and *Rhodiola crenulata*	[6,11]
Myricetin	**36**	*Bryophyllum pinnatum*	[8]
Myricetin 3-*O*-α-L-arabinopyranosyl-(1 → 2)-α-L-rhamnopyranoside	**35**	*Bryophyllum pinnatum*	[8]
Patuletin	**51**	*Kalanchoe brasiliensis*	[14]
Patuletin 3-*O*-α-L-rhamnopyranosyl-7-*O*-α-L-rhamnopyranoside	**52**	*Kalanchoe brasiliensis*	[14]
Patuletin-3-O-(4″-O-acetyl-α-L- rhamnopyranosyl)-7-O-(2‴-O-acetyl-α- L-rhamnopyranoside)	**65**	*K. brasiliensis*	[7]

(*continued on next page*)

Table 1 (*continued*)

Compound	Compound number	Species	Ref.
Patuletin-3-*O*-α-L-rhamnopyranosyl-7 *O*-(2‴-*O*-acetyl-α-*L*-rhamnopyranoside)	**66**		
Patuletin-3-*O*-(4″-*O*-acetyl-α-*L*-rhamnopyranosyl)-7-*O*-rhamnopyranoside	**67**		
p-hydroxyphenacyl-β-D-glucopyranoside	**41**	*Rhodiola crenulata*	[11]
picein	**42**	*Rhodiola crenulata*	[11]
Quercetin	**2**	*C. capitella, Kalanchoe beharensis, K. longiflora, B. pinnatum, J. sobolifera* and *O. japonicas*	[3–5,8,9]
Quercetin 3-*O*-α-D-arabinopyranoside	**26**	*C. capitella*	[3]
Quercetin 3-*O*-α-L-arabinopyranosyl-(1 → 2)-α-L-rhamnopyranoside-7-*O*-β-D-gluco-pyranoside	**37**	*Bryophyllum pinnatum*	[8]
Quercitin -3-*O*-β-D-$^4C_1$-glucopyranoside	**74**	*K. marmorata*	[7]
Quercetin 3-*O*-β-D-glucopyranoside	**28**	*C. capitella*	[3]
		K. blossfeldiana	[7]
Quercetin-3-*O*-α-*L*-arabinopyranosyl (1 → 2) α-*L*-rhamnopyranoside	**70**	*K. pinnata*	[7]
Quercetin 3-rutinoside	**48**	*Orostachys japonicas*	[5]
Quercetin-3-*O*-β-L-galactopyranoside	**54**	*Kalanchoe beharensis and K. longiflora*	[9]
Quercetin-3-*O*-α-rhamnopyranoside-7-*O*-β-D-glucopyranosyl-(1 → 3)-α-L-rhamnopyr-anoside	**29**	*Kalanchoe gastonis*	[13]
Quercetin-3-*O*-glucoside-7-*O*- rhamnoside	**56**	*K. spathulata*	[7]
Quercitrin	**64**	*K. gracilis*	[7]
Rhodionin	**12**	*Rhodiola sachalinensis.*	[6]
Rhodiosin	**13**		
Salidroside	**16**	*Rhodiola crenulata, Rhodiola sachalinensis.*	[6,11]
Syringic acid-β-D-glucopyranosyl ester	**38**	*Bryophyllum pinnatum*	[8]
Tyrosol	**43**	*Rhodiola sachalinensis, Rhodiola crenulata*	[6,11]

kaempferol 3-*O*-galactopyranosy1-(1 → 2)-*O*-α-L-rhamnopyranoside (22) isolated from *Jovibarba sobolifera* [4], kaempferol-3-*O*-β-D-glucopyranosyl-7-*O*-α-*L*-rhamnopyranoside (20) also isolated from *Rhodiola rosea* [12], 11-*O*-(4′-*O*-methyl galloyl)-bergenin (23), 4-methoxy-3, 5 dihydroxy methyl benzoate (24), kaempferol 3-*O*-α-D-arabinopyranoside (25), Quercetin 3-*O*-α-D-arabinopyranoside (26) and 11-*O*-galloyl bergenin (27) isolated from *C. capitella* [3], Quercetin 3-*O*-β-D-glucopyranoside (28), isolated from *C. capitella* [3]and *K. blossfeldiana* [7] Quercetin 3-*O*-α-rhamnopyranoside-7-*O*-β-D-glucopyranosyl-(1 → 3)-α-L-rhamnopyranoside (29), Apigenin-6-C-β-D-glucopyranosyl-8-C-β-D-glucopyranosyl (vicenin-2) (30) isolated from *Kalanchoe gastonis* [13], 4′-*O*-β-D-glucopyranosyl-cis-*p*-coumaric acid (31), Acacetin-7-*O*-α-L-rhamnopyranosyl-(1 → 6)-β-D-glucopyranoside (32), Diosmetin 7-*O*-α-L-rhamnopyranosyl-(1 → 6)-β-D-glucopyranoside (33), kaempferol 3-*O*-α-L-arabinopyranosyl-(1 → 2)-α-L-rhamnopyranoside (34), Myricetin-3-*O*-α-L-arabinopyranosyl-(1 → 2)-α-L-rhamnopyranoside (35), Myricetin (36), Quercetin 3-*O*-α-L-arabinopyranosyl-(1 → 2)-α-L-rhamnopyranoside-7-*O*-β-D-glucopyranoside (37) and Syringic acid-β-D-glucopyranosyl ester (38) isolated from *Bryophyllum pinnatum* [8], 2-(4-hydroxyphenyl)-ethyl-*O*-β-D-glucopyranosyl-6-*O*- β -D-glucopyranoside (39), Icariside D2 (40), *p*-hydroxyphenacyl-β-D-glucopyranoside (41) and picein (42), Tyrosol (43) isolated from *Rhodiola crenulata* and *Rhodiola sachalinensis* [6] [11], Herbacetin-3-*O*-β-D-glucopyranosyl-7-*O*-α-L-rhamnopyranoside (44), Herbacetin-8-O-β-D-glucopyranoside (45), and kaempferol-3-*O*-β-D-glucopyranoside-(2 → 1)-β-D-xylopyranoside (46) from *Rhodiola rosea* [12], Kaempferol 3-rutinoside (47) and Quercetin 3-rutinoside (48) from *Orostachys japonicas* [5], kaempferol-3, 7-di-*O*-glucoside (49) and kaempferol-3-rhamnosyl-7-glucoside (50) from *O. margaritifolius* [5], Patuletin (51) from Kalanchoe brasiliensis [14] and *K. spathulata* [7], Patuletin 3-*O*-α-L-rhamnopyranosyl-7-*O*-α-L-rhamnopyranoside (52) from *Kalanchoe brasiliensis* [14] and from *K. spathulata* [7], kampferol-3,7-di-*O*-α-L-rhamnopyranoside (53), Quercetin-3-*O*-β-L-galactopyranoside (54) and kampferol-3-*O*-α-L-rhamnopyranoside (55) from *Kalanchoe beharensis* and *K. longiflora* [9],Quercetin-3-*O*-glucoside-7-*O*- rhamnoside (56) and Kaempferol-3-*O*-rhamnoside (57) from *K. spathulata* [7], Eupafolin-4'-*O*-rhamnoside (58), Eupafolin-3-7 di-*O*-rhamnoside (59), Eupafolin-3-*O*-rhamnosyl-7-*O*-(4-*O*- acetylrhamnoside) (60), Eupafolin-3-*O*-(3-*O*acetylrhamnosyl)-7-*O*-(3-*O*acetylrhamnoside) (61), Luteolin (62) and Eupafolin (63) from *K. gracilis* [7], Quercitrin (64) from *K. gracilis, K. pinnata* and *K. blossfeldiana* [7],Patuletin-3-*O*-(4"-*O*-acetyl-α-*L*- rhamnopyranosyl)-7-*O*-(2"'-*O*-acetyl-α- L-rhamnopyranoside) (65), Patuletin-3-*O*-α-L-rhamnopyranosyl-7 *O*-(2"'-*O*-acetyl-α-*L*-rhamnopyranoside) (66) and Patuletin-3-*O*-(4"-*O*-acetyl-α-*L*-rhamnopyranosyl)-7-*O*-rhamnopyranoside (67) from *K. brasiliensis* [7], 4""-acetylsagittatin A (68) from *K. streptantha* [7], Kapinnatoside (69) and Quercetin-3-*O*-α-*L*-arabinopyranosyl (1→ 2) α-*L*-rhamnopyranoside (70) from *K. pinnata* [7], 8-methoxyquercetin-3,7-di-*O*- rhamnopyranoside (71) and 8-methoxykaempferol-3,7-di-*O*- rhamnopyranoside (72) from *K. brasiliensis*, *K. pinnata* & *K. gastonisbornieri* [7], Isorhamnetin-3-O-α-L-1C4-rhamnopyranoside, 4'-methoxy-myricetin-3-O-α-L-1C4-rhamnopyranoside (73) and Quercitin -3-*O*-β-D-$^4C_1$-glucopyranoside (74) from *K. marmorata* [7], Kaempferitrin (75), Kaempferol 3-O-α-L-(2-acetyl)rhamnopyranoside-7-*O*-α-L-rhamnopyranoside (76), Kaempferol 3-*O*-α-L-(3-acetyl)rhamnopyranoside-7-*O*-α-L-rhamnopyranoside (77), Kaempferol 3-*O*-α-L-(4-acetyl)rhamnopyranoside-7-*O*-α-L-rhamnopyranoside (78), Kaempferol 3-*O*-α-L-(4-acetyl)rhamnopyranoside-7-*O*-α-L-rhamnopyranoside (79), and α-rhamnoisorobin (80) from *Bryophyllum pinnatum* [7] and 3′,4′-dimethoxy quercetin (81) from *K. pinnata* [7]. Table 2.

2.2. Sterols and terpenoidal compounds (Table 2)

β-sitosterol-3-*O*-β-D-galactopyranoside (82), daucosterol (83) and ursolic acid (84) from of *Sedum caeruleum.* [10], Stigmsata-5-en-3β-ol (85), α-amyrin- β-D-glucopyranoside (86), and a new compound Stigmast-4, 20 (87), 23-trien-3-one (88) have been isolated from *Bryophyllum pinnatum* [15], stigmasterol (89) from *Bryophyllum pinnatum* [16]. Table 3.

Table 2
Sterols and terpenoidal compounds isolated from family Crassulaceae.

Compound Name	Compound number	Species	Ref.
β-sitosterol-3-*O*-β-D-galactopyranoside	**83**	*Sedum caeruleum*	[10]
Daucosterol	**84**		
Ursolic acid	**85**		
Stigmsata-5-en-3β-ol	**86**		
α-amyrin- β-D-glucopyranoside	**87**		
Stigmast-4, 20 (22), 23-trien-3-one	**88**	*Bryophyllum pinnatum*	[15]
stigmasterol	**89**	*Bryophyllum pinnatum*	[16]

Table 3
Cardenolides &bufadienolides isolated from family Crassulaceae.

Compound Name	Compound number	Species	Ref.
Bryophyllin A	**90**	Bryophyllum pinnatum	[8,17]
Bersaldegenin-1, 3, 5-orthoacetate	**91**		
Bersaldegenin-1-acetate	**92**		
Bersaldegenin-3-acetate	**93**		
kalantubolide A	**94**	Kalanchoe tubiflora	[18]
kalantubolide B	**95**		
kalantuboside A	**96**		
kalantuboside B	**97**		
Hellibrigenin-3-acetate.	**98**	*K. lanceolate*	[7]
Bersaldegenin-1,3,5-orthoacetate	**99**	*K. daigremontiana* and *K. tubiflora,*	[7]
Daigremontianin	**100**	*K. tubiflora*	[7]
Kalanchoside A	**101**	*K. gracilis*	[7]
Kalanchoside B	**102**		
Kalanchoside C	**103**		
Kalanhybrin A	**104**	*K. hybrid*	[7]
Kalanhybrin B	**105**		
Kalanhybrin C	**106**		
Daigredorigenin-3-acetate	**107**		

2.3. Cardenolides &bufadienolides (Table 3)

Bryophyllin A (90), bersaldegenin-1, 3, 5-orthoacetate (91), bersaldegenin-1-acetate (92) and bersaldegenin-3-acetate (93) in Bryophyllum pinnatum leaves. [8,17], *kalantubolide* A (94) and kalantubolide B (95), and two bufadienolide glycosides, kalantuboside A (96) and kalantuboside B (97), were isolated and characterized from *Kalanchoe tubiflora* [18]., Hellibrigenin-3-acetate (98) from *K. lanceolate* [7], Bersaldegenin-1,3,5-orthoacetate (99) from *K. daigremontiana* and *K. tubiflora* [7], Daigremontianin (100) from *K. tubiflora* [7], Kalanchoside A (101), Kalanchoside B (102) and Kalanchoside C (103) from *K. gracilis* [7], Kalanhybrin A (104), Kalanhybrin B (105), Kalanhybrin C (106) and Daigredorigenin-3-acetate (107) from *K. hybrid* [7].

3. Biological and pharmacological activities

A review of literature revealed that Family *Crassulacae* had several activities such as: Anti-oxidant, antihyperglycemic, antimicrobial, antiulcerogenic, cytotoxic/anti-cancer, anti-inflammatory & anti-nociceptive activity. Other pharmacological activities include, hepatoprotective, analgesic, anti-arthritic, anti-malarial, antimutagenic, insecticidal, anti-thrombolytic, antihypertensive and myometrial activities.

4. Anti-oxidative activity

Twelve plants of family Crassulaceae having anti-oxidant activity. *Echeveria kimnachii* (EK) and *Echeveria subrigida* (ES) are interesting sources of antioxidant compounds (e.g., phytosterols, phenolics and vitamin E). the highest antioxidant activities were for ethyl acetate fractions by DPPH (inhibition %: EK = 67.5 and ES = 95.1) [2]. The *n*-butanol extract of *Sedum caeruleum* exhibited the highest antioxidant activity (IC_{50} value: 28.35 ± 1.22 mg/mL in DPPH assay [10]. Kaempferol (IC_{50} = 3.97 ± 0.10 μg/mL) and quercetin (IC50 = 4.53 ± 0.10 μg/mL) exhibited similar activity against DPPH radicals comparable to L-ascorbic acid (IC_{50} = 2.13 ± 0.08 μg/mL) which was used as a positive control, both compounds have been isolated from different parts of *Jovibarba sobolifera* [4]. The butanolic fraction of *Sedum villosum* has the potent antioxidant activity to β-carotene bleaching method (EC_{50} = 0.35 ± 0.01 mg/ml) [19]. *Kalanchoe pinnata* extract displayed significant DPPH radical scavenging activity which increased with increasing concentration of the extract and the IC_{50} value for the extract was found to be 6.80 (μg/ml) [20]. The IC_{50} values of *Kalanchoe crenata* of Benzene (BE), Chloroform (CE), Acetone (AE) and Ethanol (EE) extracts are 178, 156, 120 and 90 μg/ml respectively in leaves. And the IC_{50} values of *K. crenata* of BE, CE, AE and EE are 192, 180,160,116 μg/ml respectively in stems. α-rhamnoisorobin which was isolated from *Bryophyllum pinnatum* was the most active antioxidant compounds (IC_{50} = 0.71 μg/ml) [21]. Chloroform fractions of *Kalanchoe gracilis* exhibited a good antioxidant activity with IC_{50} = 136.85 ± 2.32 μg/ml [22]. *Rhodiola imbricata* root extract showed the highest antioxidant capacities [23]. The aqueous and the alcoholic extract of *Bryophyllum calycinum* Salibs have interesting antimicrobial and potential free radical scavenging activity. The results of DPPH method showed 50% inhibition rate at the 144.23 μg/ml and 117.42 μg/ml with aqueous and alcoholic extract, respectively [24].

5. Antihyperglycemic activity

Three plants of family Crassulaceae having anti-hyperglycemic activity. *Rhodiola rosea* (10 mg/paw) has an effect similar to gabapentin (20 mg/paw) decreases the hyperalgesic and allodynic processes in diabetic rats [25]. *Sedum dendroideum* (SD) has hypoglycemic potential in both Diabetes Mellitus I and Diabetes Mellitus

II [26]. The dichloromethane (DCM) fraction of *Kalanchoe pinnata* demonstrates excellent insulin secretagogue action and the fasting blood glucose values were reduced to 116 mg/dl from 228 mg/dl on treatment with 10 mg/kg body weight of DCM fraction [27].

6. Antimicrobial and antiviral activities

The chloroform extract at 128 mg/ml of *Sedum caeruleum* showed a mild antibacterial activity [10]. Herbacetin-3-*O*-α-L-rhamnopyranosyl-8-*O*-α-D-lyxo-pyranoside. Gossypetin-3-*O*-β-D-glucopyranosyl-8-*O*-β-D-xylopyranoside and other compounds isolated from *Sedum aizoon* L. showed higher antibacterial activity against Gram positive than Gram negative bacteria [28]. *Bryophyllum pinnatum* and some of its isolated compounds have interesting antimicrobial properties [21]. *Bryophyllum pinnatum* stem would be used as an antimicrobial agent. *Staphylococcus aureus* showed the lowest minimum inhibitory concentration (MIC) of 6.29 mg/ml in the methanol extract, while *Salmonella typhi*, showed the highest MIC of 9.98 mg/ml in the aqueous extract (significant at $P < 0.01$) [29]. Aqueous and alcoholic of *Bryophyllum calycinum* Salibs showed significant antibacterial activity [24]. The antiviral activities of the juice of certain species belonging to the genera *Kalanchoe*; *K. blossfeldiana*; *K. beharensis*; *K. waldheimii* and *K. pinnata* were tested and shown high virus neutralizing activity [7].

7. Antiulcerogenic activity

The aqueous extract of *Bryophyllum pinnatum* (Lam.) showed a significant gastro protective action in indomethacin-induced ulcer models [30] and the herbs of *Orostachys japonicus* (Crassulaceae) have been used to treat gastric ulcer or hemorrhage [5].

8. Cytotoxic/anti-cancer activity

An isolated compound myricetin-3-*O*-β-D-glucopyranoside from *Sedum aizoon* L. exhibited moderate cytotoxic activities. The *in vitro* anti-proliferative activities against HepG2, MCF-7 and A549 tumor cell lines were also evaluated. The result suggested exhibited moderate cytotoxic activities with IC_{50} values of 46.30, 75.27 and 49.76 μmol/L, respectively [28], that the extract of *Kalanchoe pinnata* showed cytotoxic activity against brine shrimp nauplii and LC_{50} value was 50 μg/ml [20]. A methanol extract from *Bryophyllum laetivirens* reverses etoposide resistance in A549 lung cancer cells though downregulation of NF-κB, leading to decreased transcription and expression of P-gp, which eventually promotes F14 extract-mediated apoptosis [31]. The extract of *Kalanchoe tubiflora* inhibits cell proliferation and reduces cell viability through two mechanisms. First, it disrupts centrosome integrity and induces multi polarity; second, it perturbs chromosome alignment at metaphase [32]. The herbs of *Orostachys japonicus* have been used to treat gastric cancer [5]. The EtOAc soluble fraction of *Orostachys japonicus* showed the highest anti-cancer activity in AGS human gastric cancer cells; this involved inhibition of the proliferation of AGS cells by inducing apoptosis and cell cycle arrest [33]. The presence of anticancer and anti-HPV an activity in *Bryophyllum pinnata* leaves that can be further exploited as a potential anticancer, anti-HPV therapeutic for treatment of HPV infection and cervical cancer [34]. Bufadienolide glycosides from *Kalanchoe tubiflora* showed strong cytotoxicity against four human tumor cell lines (A549, Cal-27, A2058, and HL-60) with IC_{50} values ranging from 0.01 μM to 10.66 μM [18]. The crude petroleum ether and aqueous extracts of *kalanochoe pinnata* possessed both cytotoxic and antifungal activities [35]and the application of the aqueous extract of *Sedum sarmentosum* to the HepG2 cell culture caused a significant, dose-dependent inhibition of cancer cell growth [36].

9. Anti-inflammatory & anti-nociceptive activity

Rhodiola rosea had anti-inflammatory and anti-nociceptive activities in animal models [25]. The dichloromethane and hexane fractions of *Orostachys japonicus* may be potent natural protective agents against oxidative disorders caused by LPS-stimulated inflammation [37]. Stem extract of *Kalanchoe pinnata* possesses anti-inflammatory effects [38]. Stigmast-4, 20 (21), 23-trien-3-one which is a new compound from *Bryophyllum pinnatum* revealed that the anti-inflammatory of aqueous extract are mainly due to the presence of this steroidal compound [15]. And the chloroform fractions of *Kalanchoe gracilis* exhibited good anti-inflammatory activity, and inhibited the growth of HepG2 cells [22].

10. Miscellaneous activities

10.1. Hepatoprotective activity

Sedum sarmentosum prevents the D-GalN/LPS— induced fulminant hepatic failure [39].

10.2. Analgesic activity

The Stigmast-4, 20 (21), 23-trien-3-one which is a new compound from *Bryophyllum pinnatum* revealed a significant analgesic effect [15].

10.3. Anti-arthritic activity

Crassula capitella is a new natural and abundant source for 11-*O*-(4′-*O*-methyl galloyl)-bergenin for resolving chronic inflammatory diseases as Rheumatoid arthritis through antioxidant, anti-inflammatory and membrane stabilizing mechanism [3].

10.4. Anti-malarial activity

Orostachys japonicus ethanol extract exhibited a very promising anti-plasmodial activity *in vitro*. Not only an excellent inhibitory activity on *Plasmodium falciparum* growth, but also high selectivity and low cytotoxicity to human cells. These results support the development of the compound as an active principle in novel anti-malarial drugs [40].

10.5. Antimutagenic activity

The hydroethanolic leaf extract of *Bryophyllum pinnatum* possesses anti-diarrheal activity possibly mediated by interaction with β adrenoceptor, muscarinic cholinergic receptor and nitric oxide pathway [41].

10.6. Insecticidal activity

Methanolic extracts and isolates of *Kalanchoe beharensis* and *Kalanchoe longiflora* were tested for their insecticidal activity against cotton leaf worm, *Spodoptera littoralis* [9].

10.7. Anti-thrombolytic activity

The thrombolytic activity of the extract of *Kalanchoe pinnata* was investigated that the percentage of clot lysis were 3.38, 10.38 and 15.73 at concentration of 500 μg, 800 μg and 1000 μg respectively [20].

10.8. Antihypertensive activity

There is a significant anti-hypertensive effects of aqueous extract of the leaves of *Kalanchoe pinnata* in salt hypertensive rats [42].

10.9. Myometrial activity

Leaf juice of *Bryophyllum pinnatum* and its flavonoid fraction are most effective in relaxing myometrial strips by inducing frequency [43].

10.10. Sedative activity

Daigremontianin and bersaldegenin- 1, 3, 5- orthoacetate that were isolated from *K. daigremontiana* and *K. tubiflora* had shown a strong sedative effect in mice [7].

11. Conclusion

There is an increasing attention worldwide for herbal medicine specially those which had been used as ornamental plants. Lately, deep pharmacological assays had been done to investigate their medicinal value. This literature survey revealed that family *Crassulaceae* had been thoroughly used in traditional medicine in different areas along the world. Also, this family contains many bioactive constituents as flavonoids, sterols, triterpenoids, phenolic components and bufadenolides. All these phytoconstituents proved to possess different biological activities Anti-oxidant, anti-hyperglycemic, antimicrobial, antiulcerogenic, cytotoxic/anti-cancer, anti-inflammatory & anti-nociceptive activity, hepatoprotective, analgesic, anti-arthritic, anti-malarial, antimutagenic, insecticidal, anti-thrombolytic, antihypertensive and myometrial activities. We are assured that further studies may be needed to declare more phytoconstituents and biological activities. Also clinical trials had not been verified up till now so we would like to suggest that researchers all over the world may invade this unrivaled area of research.

Conflicts of interest

The authors have no conflict to declare.

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