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Phytochemical and Therapeutic Profile *of Aloe vera*

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Abstract

Aloe vera (L.) Burm. f. (Family Liliaceae) is an evergreen perennial succulent plant widely used from antiquity. *Aloe vera* contains various carbohydrate polymers, notably glucomannans, along with a range of other organic and inorganic components. Phenolic compounds have been identified so far as chromone, anthraquinone or anthrone derivatives. Three distinct preparations of aloe plants are mostly used in medicinal practices that are quite different in their chemical composition and their therapeutic properties, aloe latex (aloe); aloe gel (*Aloe vera*); and, aloe whole leaf (aloe extract). Aloe latex is used for its laxative effect; aloe gel is used topically for skin ailments, such as wound healing, psoriasis, genital herpes and internally by oral administration in diabetic and hyperlipidaemic patients and to heal gastric ulcers; and, aloe extract is potentially useful for cancer and AIDS. *Aloe vera* possesses several pharmacological properties such as promoting and healing wound and burn, frost-bite healing, with addition to having antiinflammatory, antifungal, hypoglycemic and gastroprotective properties. This review explored the phytochemical and pharmacological knowledge as well as several promising aspects for research on aloe.

Keyword: *Aloe vera*, Aloe, Indian aloe, Kumari, Ghritakumari, Aloin

1. Introduction

Aloe vera (L.) Burm. f. is not a cactus but is a cactus like an indigenous medicinal, herb growing in tropical and subtropical latitudes with very good economic potential. There are more than 600 known species of Aloe (Family Liliaceae) [1], many of which have been used as botanical medicines in many countries for thousands of years. Some species of aloe have enlisted and shown in Table 1.

This perennial species has a number of synonyms: *Aloe barbadensis* Miller; *Aloe indica* Royle; *Aloe perfoliata* L. var. vera, and *Aloe vulgaris* Lam., with common names including Curacao aloe (commercial source), Indian aloe, ghikawar; ghritakumari; gwar-patha; kumari (Hind.), Chinese aloe laloi, first aid plant. The species name vera means "true" or "genuine". The species was first described by Carl Linnaeus in 1753 as *Aloe perfoliata* var. vera, and was described again in 1768 by Nicolaas Laurens Burman as *Aloe vera* in Flora Indica [2]. Techniques based on DNA sequence comparison and ISSR profiling suggests that it is relatively closely related to *Aloe perryi*, a species that is endemic to Yemen; and some other species like *Aloe forbesii*; *Aloe inermis; Aloe scobinifolia; Aloe sinkatana* and *Aloe striata*. Most commonly used species include: *Aloe arborescens, Aloe aristata, Aloe nyeriensis, Aloe variegata, Aloe wildii*.

2. Background and History

Aloes have been used therapeutically, certainly since Roman times and perhaps long before [3]. It is mentioned both in the Bible and by the ancient Egyptians. The topical and internal effects of aloes have been known since ancient times. Nefertite (1353 B.C.) and Cleopatra (69–30 B.C.) two Egyptian queens, used aloes as a beauty aid. Aloes were used by Pliny the Elder, Celsus, Galen and other famous physicians to treat wounds and gastrointestinal disturbances. Aloe's use

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Table 1: Different species of Aloe

1. *Aloe aageodonta* L.E.Newtor	2. *Aloe abhaica* Lavranos & Collenette	3. *Aloe abyssicola* Lavranos & Bilaidi	4. *Aloe aculeata* Pole-Evans
5. *Aloe acutissima* H.Perrier	6. *Aloe adigratana* Reynolds	7. *Aloe affinis* A.Berger	8. *Aloe africana* Miller
9. *Aloe ahmarensis* Favell et al.	10. *Aloe albida* (Stapf) Reynolds	11. *Aloe albiflora* Guill.	12. *Aloe albovestida* S.Carter & Brandham
13. *Aloe aldabrensis* (Marais) L.E.Newton & G.D.Powley	14. *Aloe alfredii* Rauh	15. *Aloe alooides* (Bolus) van Druten	16. *Aloe ambigens* Chiovenda
17. *Aloe amicorum* L.E.Newton	18. *Aloe amudatensis* Reynolds	19. *Aloe andongensis* Baker	20. *Aloe andringitrensis* H.Perrier
21. *Aloe angelica* Pole-Evans	22. *Aloe angolensis* Baker	23. *Aloe anivoranoensis* (Rauh & GHebding) L.E.Newton	24. *Aloe ankaranensis* Rauh & Mangelsdorff
25. *Aloe ankoberensis* M.G.Gilbert & Sebsehe	26. *Aloe antandroi* (Decary) H.Perrier	27. *Aloe antsingyensis* (Léandri) L.E.Newton	28. *Aloe arborescens* Miller
29. *Aloe archeri* Lavranos	30. *Aloe arenicola* Reynolds	31. *Aloe argenticauda* Merxmüller & Giess	32. *Aloe aristata* Haworth
33. *Aloe armatissima* Lavranos & Collenette	34. *Aloe asperifolia* A.Berger	35. *Aloe babatiensis* Christian & I.Verdoorn	36. *Aloe bakeri* Scott-Elliot
37. *Aloe ballii* Reynolds	38. *Aloe barberae* Dyer	39.*Aloe bargalensis* Lavranos	40. *Aloe balevenokensis* (Rauh & Gerold) L.E.Newton
41. *Aloe bella* G.D.Rowley	42. *Aloe bellatula* Reynolds	43. *Aloe berevoana* Lavranos	44. *Aloe bernadettae* Castillon
45. *Aloe bertemariae* Sebsebe & Diali	46. *Aloe betsileensis* H.Perrier	47. *Aloe bicomitum* L.C.Leach	48. *Aloe boiteaui* Guill.
49. *Aloe boscawenii* Christian	50. *Aloe bosseri* Castillon	51. *Aloe bowiea* Schultes & Schultes f.	52. *Aloe brachystachys* Baker
53. *Aloe branddraaiensis* Groenewald	54. *Aloe brandhamii* S.Carter	55. *Aloe brevifolia* Miller	56. *Aloe breviscapa* Reynolds
57. *Aloe broomii* Schönland	58. *Aloe brunneodentata* Lavranos & Collenette	59. *Aloe bruneostriata* Lavranos & S.Carter	60. *Aloe buchananii* Baker
61. *Aloe buchlohii* Rauh	62. *Aloe buettneri* A.Berger	63. *Aloe buhrii* Lavranos	64. *Aloe bukobana* Reynolds
65. *Aloe bulbicaulis* Christian	66. *Aloe bulbifera* H.Perrier	67. *Aloe bullockii* Reynolds	68. *Aloe burgerforstensis* Reynolds
69. *Aloe bussei* A.Berger	70. *Aloe calcairophila* Reynolds	71. *Aloe calidophila* Reynolds	72. *Aloe cameronii* Hemsley
73. *Aloe camperi* Schweinfurth	74. *Aloe canarina* S.Carter	75. *Aloe cannellii* L.C.Leach	76. *Aloe capitata* Baker
77. *Aloe capmananmbatoensis* Rauh & Gerold	78. *Aloe carnea* S.Carter	79. *Aloe castanea* Schönland	80. *Aloe castellorum* J.R.I.Wood
81. *Aloe catengiana* Reynolds	82. *Aloe caphalophora* Lavranos & Collenette	83. *Aloe chabaudii* Schönland	84. *Aloe cheranganiensis* S.Carter & Brandham

Continued

Table 1: *Continued*

85. *Aloe chloranta* Lavranos	86. *Aloe chortolirioides* A.Berger	87. *Aloe christianii* Reynolds	88. *Aloe chrysostachys* Lavranos & L.E.Newton
89. *Aloe ciliaris* Haworth	90. *Aloe cirtina* S.Carter & Brandham	91. *Aloe classenii* Reynolds	92. *Aloe claviflora* Burchell
93. *Aloe collenetteae* Lavranos	94. *Aloe collina* S.Carter	95. *Aloe commixta* A.Berger	96. *Aloe comosa* Marloth & A.Berger
97. *Aloe compressa* H.Perrier	98. *Aloe comptonii* Reynolds	99. *Aloe confusa* Engler	100. *Aloe congdonii* S.Carter
101. *Aloe conifera* H.Perrier	102. *Aloe cooperi* Baker	103. *Aloe corallina* I.Verdoorn	104. *Aloe crassipes* Baker
105. *Aloe cremersii* Lavranos	106. *Aloe cremnophila* Reynolds & P.R.O. Bally	107. *Aloe cryptoflora* Reynolds	108. *Aloe cryptopoda* Baker
109. *Aloe cyrtophylla* Lavranos	110. *Aloe daberonisana* van Jaarsveld	111. *Aloe dawei* A.Berger	112. *Aloe debrana* Christian
113. *Aloe decorsei* H.Perrier	114. *Aloe decurva* Reynolds	115. *Aloe delphinensis* Rauh	116. *Aloe deltoideodonta* Baker var. candidans H.Perrier
117. *Aloe deltoideodonta* Baker	118. *Aloe descoingsii* Reynolds	119. *Aloe deserti* A.Berger	120. *Aloe dewetii* Reynolds
121. *Aloe dewinteri* Giess	122. *Aloe dhufarensis* Lavranos	123. *Aloe dichotoma* Masson	124. *Aloe dinteri* A.Berger
125. *Aloe diolii* L.E.Newton	126. *Aloe distans* Haworth	127. *Aloe divaricata* A.Berger	128. *Aloe doei* Lavranos
129. *Aloe dominella* Reynolds	130. *Aloe dorotheae* A.Berger	131. *Aloe duckeri* Christian	132. *Aloe dyeri* Schönland
133. *Aloe ecklonis* Salm-Dyck	134. *Aloe edentata* Lavranos & Collenette	135. *Aloe elata* S.Carter & L.E.Newton	136. *Aloe elegans* Todaro
137. *Aloe elgonica* Bullock	138. *Aloe ellenbeckii* A.Berger	139. *Aloe eminens* Reynolds & P.R.O.Bally	140. *Aloe enotata* L.C.Leach
141. *Aloe eremophila* Lavranos	142. *Aloe erensii* Christian	143. *Aloe ericetorum* Bosser	144. *Aloe erythrophylla* Bosser
145. *Aloe esculenta* L.C.Leach	146. *Aloe eumassawana* S.Carter et al.	147. *Aloe excelsa* A.Berger	148. *Aloe falcata* Baker
149. *Aloe ferox* Miller	150. *Aloe fibrosa* Lavranos & L.E.Newton	151. *Aloe fievetii* Reynolds	152. *Aloe fimbrialis* S.Carter
153. *Aloe fleurentiniorum* Lavranos & L.E.Newton	154. *Aloe fleuretteana* Rauh & Gerold	155. *Aloe flexilifolia* Christian	156. *Aloe forbesii* Balfour f.
157. *Aloe fosteri* Pillans	158. *Aloe fouriei* D.S.Hardy & Glen	159. *Aloe fragilis* Lavranos & Röösli	160. *Aloe framesii* L.Bolus
161. *Aloe francombei* L.E.Newton	162. *Aloe frisii* Sebsebe & M.G.Gilbert	163. *Aloe fulleri* Lavranos	164. *Aloe gariepensis* Pillans
165. *Aloe gerstneri* Reynolds	166. *Aloe gilbertii* T.Reynolds ex Sebsebe & Brandham	167. *Aloe gillettii* S.Carter	168. *Aloe glabrescens* (Reynolds & P.R.O.Bally) S.Carter & Brandham
169. *Aloe glauca* Miller	170. *Aloe globuligemma* Pole-Evans	171. *Aloe gossweileri* Reynolds	172. *Aloe gracilicaulis* Reynolds & R.P.O.Bally
173. *Aloe gracilis* Haworth	174. *Aloe gradidentata* Salm-Dyck	175. *Aloe grata* Reynolds	176. *Aloe greatheadii* Schönland

Continued

Table 1: *Continued*

177. *Aloe greenii* Baker	178. *Aloe grisea* S.Carter & Brandham	179. *Aloe guerrae* Reynolds	180. *Aloe guillaumetii* Cremers
181. *Aloe haemanthifolia* A.Berger & Marloth	182. *Aloe hardyi* Glen	183. *Aloe harlana* Reynolds	184. *Aloe haworthioides* Baker
185. *Aloe hazeliana* Reynolds	186. *Aloe helenae* Danguy	187. *Aloe heliderana* Lavranos	188. *Aloe hemmingii* Reynolds & P.R.O.Bally
189. *Aloe hendrickxii* Reynolds	190. *Aloe hereroensis* Engler	191. *Aloe heybensis* Lavranos	192. *Aloe hijazensis* Lavranos & Collenette
193. *Aloe hildebrandtii* Baker	194. *Aloe hlangapies* Groenewald	195. *Aloe howmanii* Reynolds	196. *Aloe humbertii* H.Perrier
197. *Aloe humilis* (L.) Miller	198. *Aloe ibitiensis* H.Perrier	199. *Aloe imalotensis* Reynolds	200. *Aloe* x *imerinensis* Bosser
201. *Aloe immaculata* Pillans	202. *Aloe inamara* L.C.Leach	203. *Aloe inconspicua* Plowes	204. *Aloe inermis* Forssk°al
205. *Aloe integra* Reynolds	206. *Aloe inyangensis* Christian	207. *Aloe isAloensis* H.Perrier	208. *Aloe itremensis* Reynolds
209. *Aloe jacksonii* Reynolds	210. *Aloe jocunda* Reynolds	211. *Aloe juvenna* Brandham & S.Carter	212. *Aloe* x *keayi* Reynolds
213. *Aloe kedongensis* Reynolds	214. *Aloe kafaensis* M.G.Gilbert & Sebsebe	215. *Aloe keithii* Reynolds	216. *Aloe ketebrowniorum* L.E.Newton
217. *Aloe khamiensis* Pillans	218. *Aloe kilifiensis* Christian	219. *Aloe kniphofioides* Baker	220. *Aloe krapohliana* Marloth
221. *Aloe kraussii* Baker	222. *Aloe kulalensis* L.E.Newton & Beentje	223. *Aloe labworana* (Reynolds) S.Carter	224. *Aloe laeta* A.Berger
225. *Aloe lateritia* Engler	226. *Aloe lavranosii* Reynolds	227. *Aloe leachii* Reynolds	228. *Aloe leandrii* Bosser
229. *Aloe leedalii* S.Carter	230. *Aloe lensayuensis* Lavranos & L.E.Newton	231. *Aloe lepida* L.C.Leach	232. *Aloe leptosiphon* A.Berger
233. *Aloe lattyae* Reynolds	234. *Aloe lindenii* Lavranos	235. *Aloe linearifolia* A.Berger	236. *Aloe lineata* (Aiton) Haworth
237. *Aloe littoralis* Baker	238. *Aloe lolwensis* L.E.Newton	239. *Aloe lomatophylloides* Balfour f.	240. *Aloe longistyla* Baker
241. *Aloe luapulana* L.C.Leach	242. *Aloe lucile-allorgeae* Rauh	243. *Aloe luntii* Baker	244. *Aloe lutestcens* Groenewald
245. *Aloe macleayi* Reynolds	246. *Aloe macra* Hawoth	247. *Aloe macrocarpa* Todaro	248. *Aloe macroclada* Baker
249. *Aloe macrosiphon* Baker	250. *Aloe maculata* Allioni	251. *Aloe marlothii* A.Berger	252. *Aloe massawana* Reynolds
253. *Aloe mawii* Chrstian	254. *Aloe mayottensis* A.Baker	255. *Aloe mcloughlinii* Christian	256. *Aloe medishiana* Reynolds
257. *Aloe megalacantha* Baker	258. *Aloe megalocarpa* Lavranos	259. *Aloe melanacantha* A.Berger	260. *Aloe melanacantha* A.Berger var. erinacea (D.S.Hardy) G.D.Rowley
261. *Aloe menachensis* (Schweinfurth) Blatter	262. *Aloe mendesii* Reynolds	263. *Aloe menyharthii* Baker	264. *Aloe metalica* Engler & Gilg
265. *Aloe meyeri* van Jaarsveld	266. *Aloe micracantha* Haworth	267. *Aloe microdonta* Chiovenda	268. *Aloe microstigma* Salm-Dyck

Continued

Table 1: *Continued*

269. *Aloe millotii* Reynolds	270. *Aloe milne-redheadii* Christian	271. *Aloe minima* Baker	272. *Aloe mitriformis* Miller
273. *Aloe modesta* Reynolds	274. *Aloe meloderana* Lavranos & Glen	275. *Aloe monotropa* I.Verdoorn	276. *Aloe monticola* Reynolds
277. *Aloe morijensis* S.Carter & Brandham	278. *Aloe mubendiensis* Christian	279. *Aloe mudenensis* Reynolds	280. *Aloe multicolor* L.E.Newton
281. *Aloe munchii* Christian	282. *Aloe murina* L.E.Newton	283. *Aloe musapana* Reynolds	284. *Aloe mutabilis* Pillans
285. *Aloe myriacantha* (Haworth) Schultes & Schultes f.	286. *Aloe mzimbana* Christian	287. *Aloe namibensis* Giess	288. *Aloe namorokaensis* (Rauh) L.E.Newton
289. *Aloe ngongensis* Christian	290. *Aloe niebuhriana* Lavranos	291. *Aloe nubigena* Groenewald	292. *Aloe nuttii* Baker
293. *Aloe nyeriensis* Christian ex I.Verdoorn	294. *Aloe occidentalis* (H.Perreier) L.E.Newton	295. *Aloe officinalis* Forssk°al	296. *Aloe oligophylla* Baker
297. *Aloe orientalis* (H.Perrier) L.E.Newton	298. *Aloe ortholopha* Christian & Milne-Redhead	299. *Aloe otallensis* Baker	300. *Aloe pachygaster* Dinter
301. *Aloe paedogona* A.Berger	302. *Aloe palmiformis* Baker	303. *Aloe paralleifolia* H.Perrier	304. *Aloe parvibracteata* Schönland
305. *Aloe parvicapsula* Lavranos & Collenette	306. *Aloe parvicoma* Lavranos & Collenette	307. *Aloe parvidens* M.G.Gilbert & Sesebe	308. *Aloe parvula* A.Berger
309. *Aloe patersonii* B.Mathew	310. *Aloe pearsonii* Schönland	311. *Aloe peckii* P.R.O.Bally & I.Verdoorn	312. *Aloe peglerae* Schönland
313. *Aloe pembana* L.E.Newton	314. *Aloe pendens* Forssk°al	315. *Aloe penduluflora* Baker	316. *Aloe percrassa* Todaro
317. *Aloe perrieri* Reynolds	318. *Aloe perryi* Baker	319. *Aloe perticola* Pole-Evans	320. *Aloe pertophila* Pillans
321. *Aloe peyrierasii* Cremers	322. *Aloe pictifolia* D.S.Hardy	323. *Aloe pillansii* L.Guthrie	324. *Aloe pirottae* A.Berger
325. *Aloe plicatilis* (L.) Miller	326. *Aloe plowesii* Reynolds	327. *Aloe pluridens* Haworth	328. *Aloe polyphylla* Schönland ex Pillans
329. *Aloe porphyrostachys* Lavranos & Collenette	330. *Aloe powysiorum* L.E.Newton	331. *Aloe pratensis* Baker	332. *Aloe pretoriensis* Pole-Evans
333. *Aloe prinslooi* I.Verdoorn & D.S.Hardy	334. *Aloe procera* L.C.Leach	335. *Aloe propagulifera* (Rauh & Rasafindratsira) L.E.Newton	336. *Aloe prostrata* (H.Perrier) L.E.Newton & G.D.Rowley
337. *Aloe pruinosa* Reynolds	338. *Aloe pseudorubroviolacea* Lavranos & Collenette	339. *Aloe pubescens* Reynolds	340. *Aloe pulcherrima* M.G.Glbert & Sebsebe
341. *Aloe purpurea* Lamarck	342. *Aloe pustuligemma* L.E.Newton	343. *Aloe* x *qaharensis* Lavranos & Collenette	344. *Aloe rabaiensis* Rendle
345. *Aloe ramosissima* Pillans	346. *Aloe rauhii* Reynolds	347. *Aloe reitzii* Reynolds	348. *Aloe retrospiciens* Reynolds & P.R.O.Bally
349. *Aloe reynoldsii* Letty	350. *Aloe rhodesiana* Rendle	351. *Aloe richardsiae* Reynolds	352. *Aloe rigens* Reynolds & P.R.O.Bally

Continued

Table 1: *Continued*

353. *Aloe rivae* Baker	354. *Aloe rivierei* Lavranos & L.E.Newton	355. *Aloe rosea* (H.Perrier) L.E.Newton & G.D.Rowley	356. *Aloe rubroviolacea* Schweinfurth
357. *Aloe ruffingiana* Rauh & Petignat	358. *Aloe rugosifolia* M.G.Gilbert & Sebsebe	359. *Aloe rupestris* Baker	360. *Aloe rupicola* Reynolds
361. *Aloe ruspoliana* Baker	362. *Aloe sabeae* Schweinfurth	363. *Aloe saundersiae* (Reynolds) Reynolds	364. *Aloe scabrifolia* L.E.Newton & Lavranos
365. *Aloe schelpei* Reynolds	366. *Aloe schilliana* L.E.Newton & G.D.Rowley	367. *Aloe schoelleri* Schweinfurth	368. *Aloe schomeri* Rauh
369. *Aloe schweinfurthii* Baker	370. *Aloe scobinifolia* Reynolds & P.R.O.Bally	371. *Aloe scorpioides* L.C.Leach	372. *Aloe secundiflora* Engler
373. *Aloe seretii* De Wildeman	374. *Aloe serriyensis* Lavranos	375. *Aloe shadensis* Lavranos & Collenette	376. *Aloe sheilae* Lavranos
377. *Aloe silicicola* H.Perrier	378. *Aloe simii* Pole-Evans	379. *Aloe sinana* Reynolds	380. *Aloe sinkatana* Reynolds
381. *Aloe sladeniana* Pole-Evans	382. *Aloe socialis* (H.Perrier) L.E.Newton & G.D.Rowley	383. *Aloe somaliensis* W.Watson	384. *Aloe soutpansbergensis* I.Verdoorn
385. *Aloe speciosa* Baker	386. *Aloe spicata* L.f.	387. *Aloe splendens* Lavranos	388. *Aloe squarrosa* Baker
389. *Aloe steffaniana* Rauh	390. *Aloe steudneri* Schweinfurth	391. *Aloe striata* Haworth	392. *Aloe striata* Haworth subsp. kerasbergensis (Pillans) Glen & D. S. Hardy
393. *Aloe striatula* Haworth	394. *Aloe suarezensis* H.Perrier	395. *Aloe subacutissima* G.D.Rowley	396. *Aloe succotrina* Allioni
397. *Aloe suffulta* Reynolds	398. *Aloe suprafoliata* Pole-Evams	399. *Aloe suzannae* Decary	400. *Aloe swynnertonii* Rendle
401. *Aloe tenuior* Haworth	402. *Aloe tewoldei* M.G.Gilbert & Sebsebe	403. *Aloe thompsoniae* Groenewald	404. *Aloe thoncroftii* Pole-Evans
405. *Aloe thraskii* Baker	406. *Aloe tomentosa* Deflers	407. *Aloe tormentorii* (Marais) L.E.Newton & G.D.Rowley	408. *Aloe tororoana* Reynolds
409. *Aloe torrei* I.Verdoorn & Christian	410. *Aloe trychyticola* (H.Perrier) Reynolds	411. *Aloe trichosantha* A.Berger	412. *Aloe trigonantha* L.C.Leach
413. *Aloe tugenensis* L.E.Newton & Lavranos	414. *Aloe turkanensis* Christian	415. *Aloe tweediae* Christian	416. *Aloe ukambensis* Reynolds
417. *Aloe umfoloziensis* Reynolds	418. *Aloe vacillans* Forssk°al	419. *Aloe vallaris* L.C.Leach	420. *Aloe vanbalenii* Pillans
421. *Aloe vandermerwei* Reynolds	422. *Aloe vaombe* Decorse & Poisson	423. *Aloe vaotsanda* Decary	424. *Aloe variegata* L.
425. *Aloe vera* (L.) Burman f.	426. *Aloe verecunda* Pole-Evans	427. *Aloe versicolor* Guill.	428. *Aloe vseyi* Reynolds
429. *Aloe viguieri* H.Perrier	430. *Aloe viridiflora* Reynolds	431. *Aloe vituensis* Baker	432. *Aloe vogtsii* Reynolds
433. *Aloe volkensii* Engler	434. *Aloe vossii* Reynolds	435. *Aloe vryheidensis* Groenewald	436. *Aloe whitcombei* Lavranos
437. *Aloe wildii* (Reynolds) Reynolds	438. *Aloe wilsonii* Reynolds	439. *Aloe wollastonii* Rendle	440. *Aloe woodii* Lavranos & Collenette
441. *Aloe wrefordii* Reynolds	442. *Aloe yavellana* Reynolds	443. *Aloe yemenica* J.R.I.Wood	444. *Aloe zebrina* Baker
445. *Aloe zombitsiensis* Rauh & M.Teissier			

was first discovered on a Sumerian clay tablet dating from 2200 B.C. as plants of great healing power. Later, in 1862, a German Egyptologist, George Ebers, discovered first detailed description of aloe's medicinal value in the Ebers Papyrus written around 1552 B.C. in Egypt. This document gives twelve formulas for mixing aloe with other agents to treat both internal and external human disorders including laxative and dermatologic preparation. Aloe was considered by the ancient Greeks to be an exclusive production of the island of Socotra, in the Indian Ocean. Aloe was first reported in Greek literature as a laxative before the first century. In the first century (41~68 AloeD.), Dioscorides wrote of its use in treating wounds, chapping, hair loss, genital ulcers, haemorrhoids, boils, mouth irritation and inflammation and and an illustration appeared in the Codex Aniciae Julianae, produced in the year CE 512 [4, 5]. In the seventh century, aloe was also used for eczema and sinusitis. Aloe is popular in traditional Ayurvedic and Chinese medicine also, from ancient era. Historical use of various aloe species by humans is well documented because it is cultivated over 3000 years. Documentation of the clinical effectiveness is also available, although it is relatively limited [6].

3. Phyto-geography and Distribution

The exact origin of *Aloe vera* is uncertain, as the species has been widely cultivated throughout the world (Fig. 1), so it is difficult to discern where it originated.

It has been suggested that naturalized stands of the species occur through North Africa in Algeria, Morocco, and Tunisia, along with the Canary and Madeira Islands. Habitats described that it was spread throughout the mediterranean region by man including the area surrounding the Mediterranean Sea in Europe, some parts of the southwestern United States, Southern Australia, and the eastern and southern parts of Africa. Its closest relatives, however, occur in Arabia, and this is its most probable area of origin. It can be found, on the lower slopes of the coastal mountains. The species was introduced to China, India, Pakistan and various parts of southern Europe in the 17th century. In India the plant is mainly found in Rajasthan and other dry belts. It also grows in coasts of Mumbai, Gujarat and South India.

Fig. 1. Aloe vera cultivation

4. Botanical Description

It is an evergreen perennial succulent plant having fleshy, sword-shaped leaves growing up to 1 meter in height. Leaves are green, tightly packed, thorny edges and are radially arranged in two or three circles. Bright yellow tubular flowers appear in a spike. The oldest and largest leaves are at the base, with leaves in the centre of the rosette formation being younger and smaller. Mature leaves can be 2–2.5 cm thick and 6–10 cm wide at the base, gradually tapering to a point at the apex. The upper leaf surface is flat or slightly dish-shaped and the lower surface rounded, with both surfaces being smooth to the touch. However, the margins of the leaf are armed with firm, spreading, triangular-shaped teeth 2–4 mm long. The unbranched flower spike carries yellow, tubular flowers. The flowers are produced in summer on a spike up to 90 cm tall, each flower pendulous, with a yellow tubular corolla 2–3 cm (0.8–1.2 in) long [7, 8] *Aloe vera* leaves are formed by a thick epidermis (skin) covered with cuticle surrounding the mesophyll, which can be differentiated into chlorenchyma cells and thinner walled cells forming the parenchyma (fillet). The parenchyma cells contain a transparent mucilaginous jelly which is referred to as gel [9].

5. Phytoconstituents

The chemistry of the aloe plant has been studied for many years. Although for the analysis of the chemical components in aloe, various methods such as fluorophotometry, thin layer chromatography, size exclusion chromatography, GC, GC/MS, HPLC, LC/MS, atomicabsorption spectrometry, counter current chromatography, capillary electrophoresis and micellar electrokinetic

chromatography etc. have been used; the HPLC method has been widely applied to analyze the components in aloe [10]. Chemical analysis reveals that *Aloe vera* contains various carbohydrate polymers, notably glucomannans, along with a range of other organic and inorganic components [11]. When the leaves of most species of Aloe are cut, more or less copious exudate appears containing phenolic compounds which can be distinguished chromatographically as over 100 major zones stained characteristic colors with different dyes. Some of the compounds in these zones have been characterized and identified so far as chromone, anthraquinone or anthrone derivatives. The second product, aloe gel, is the clear, jelly-like material from the sticky cells found in the inner tissue of the leaf. It generally doesn't contain the anthraquinone glycosides found in the latex but does contain the polysaccharides glucomannan and acemannan. Other potentially active components that have been identified include bradykininase, magnesium lactate, and salicylic acid [12–14]. The phytoconstituents of aloe are categorized and shown in Table 2.

6. Biological Activity and Therapeutic Uses

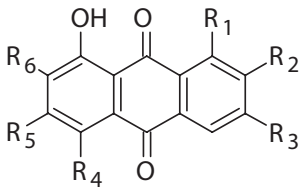
Aloe vera has a long association with herbal medicine, although it is not known when its medical applications were first discovered. Three distinct preparations of aloe plants are mostly used in a medicinal capacity that are quite different in their chemical composition and their therapeutic properties, aloe latex (aloe); aloe gel (*Aloe vera*); and, aloe whole leaf (aloe extract). Aloe latex is used for its laxative effect; aloe gel is used topically for skin ailments, such as wound healing, psoriasis, genital herpes and internally by oral administration in diabetic and hyperlipidaemic patients and to heal gastric ulcers; and aloe extract is potentially useful for cancer and AIDS. Aloe has the ability to penetrate the deepest body tissues. It has antiseptic properties, which kill bacteria, viruses and fungus. The gel of *Aloe* is potent and it is got from the leaves. This *Aloe* gel has as many as 75 nutrients, which promises good health. It stimulates the growth of new health tissues. It has calming effect on the body's nervous system and cleanses, detoxifies and normalizes the body's metabolism. It has been investigated that the gel extract of *Aloe vera* presents various pharmacological properties such as promoting and healing wound and burn, frostbite healing, with addition to having antiinflammatory, antifungal, hypoglycemic and gastroprotective properties [15]. The specific pharmacological activity and uses are summarized and depicted in Table 3.

6.1 Wound Healing

Classical use of Aloe gel is its wound healing potential and one of the first explanations of its efficacy is its high water content which can keep the wound moist and increased epithelial cell migration [3, 16]. Mannose 6-phosphate, the principal sugar component of *Aloe vera* gel, may

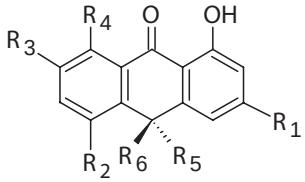
Table 2: Phytoconstituents of *Aloe vera*

Anthraquinones in *Aloe*



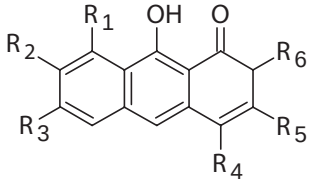
Compound	R_1	R_2	R_3	R_4	R_5	R_6
Aloe-emodin	OH	H	CH_2OH	H	H	H
Chrysophanol	OH	H	CH_3	H	H	H
Aloesaponarin I	CH_3	$COOCH_3$	OH	H	H	H
Aloesaponarin II	CH_3	H	OH	H	H	H
Laccaic acid D-methylester	OH	$COOCH_3$	OH	H	OH	H
Deoxyerythro -laccin	CH_3	H	OH	H	OH	H
Helminthosporin	OH	H	CH_3	OH	H	H

Anthranols in *Aloe*



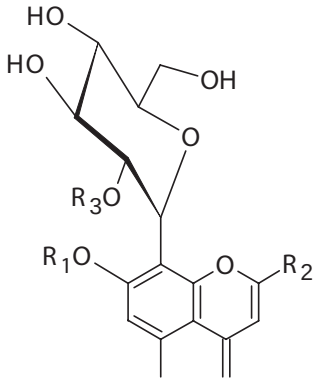
Compound	R_1	R_2	R_3	R_4	R_5	R_6
Aloin A (Barbaloin)	CH_2OH	H	H	OH	H	C-glc
Aloin B (Isobarbaloin)	CH_2OH	H	H	OH	C-glc	H
5-hydroxyaloin A	CH_2OH	OH	H	OH	C-glc	H
7-hydroxyaloin A	CH_2OH	H	OH	OH	H	H
7-hydroxyaloin B	CH_2OH	H	OH	OH	C-glc	H
(+)-homonataloin	CH_3	H	OH	OCH_3	H	C-glc
(-)-homonataloin	CH_3	H	OH	OCH_3	C-glc	H
Microdontin A	CH_2OH	H	H	OH	H	C-glc-2′-Coumaroyl
Microdontin B	CH_2OH	H	H	OH	C-glc-2′-Coumaroyl	H
10-hydroxyaloin A	CH_2OH	H	H	OH	OH	C-glc
10-hydroxyaloin B	CH_2OH	H	H	OH	C-glc	OH
8-O-methyl-7-hydroxyaloin A	CH_2OH	H	OH	OCH_3	H	C-glc
8-O-methyl-7-hydroxyaloin B	CH_2OH	H	OH	OCH_3	C-glc	H
5-hydroxyaloin A 6′-O-acetate	CH_2OH	OH	H	OH	C-glc-6′-acetyl	H

Anthranols in Aloe

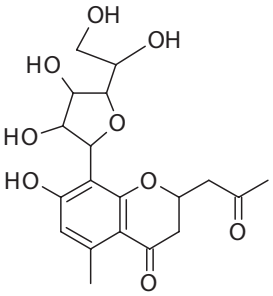


Compound	R_1	R_2	R_3	R_4	R_5	R_6
Aloesaponol I 6-O-β-Dglucoside	CH_3	$COOCH_3$	O-glc	H	OH	H
Aloesaponol III 6-O- β- D-glucoside	OH	H	O-glc	H	OH	H
Aloesaponol III 8-O- β- D-glucoside	O-glc	H	CH_3	H	H	H
Aloesaponol III 4-O- β- D-glucoside	OH	H	CH_3	O-glc	H	OH
Aloesaponol IV 4-O- β- D-glucosided-methylester	OH	H	CH_3	O-glc	H	OCH_3

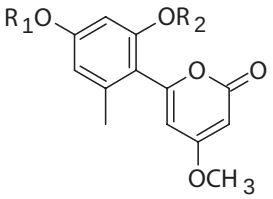
Chromones in Aloe



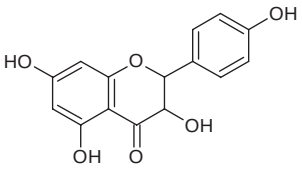
Compound	R_1	R_2	R_3
Aloesin	H	CH_2COCH_3	H
8-C-glucosyl-7-Omethyl-(S)-aloesol	CH_3		H
Isoaloeresin D	CH_3		p-(E)- coumaroyl
Aloeresin E	CH_3		(E)-cinnamoyl
7-O-methylaloeresin A	CH_3	CH_2COCH_3	p-(E)- coumaroyl
7-O-methylaloesin	CH_3	CH_2COCH_3	H



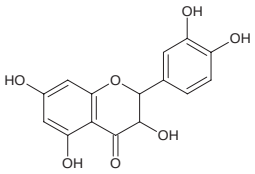
Neoaloesin A



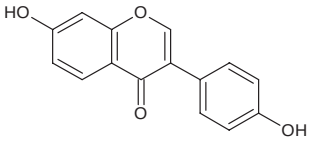
R_1= B-D-glucosyl
R_2= B-D-glucosyl-2″-p-coumaroyl



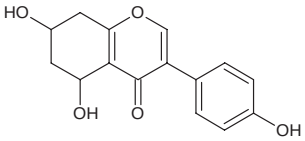
Kaempferol



Quercetin



Daidzin



Genistein

be partly responsible for the wound healing properties of the gel. *In vivo* studies have demonstrated that *Aloe vera* gel promotes wound healing by direct stimulation of macrophages and fibroblasts through the binding of mannose 6-phosphate to the growth factor receptors on the surface of the fibroblasts to increase both collagen and proteoglycan synthesis, thereby promoting tissue repair [4, 17, 18].

Furthermore, a water-soluble long-chain mannose polymer acemannan, isolated from Aloe leaves, has showd to accelerate wound healing and reduce radiation induced skin reactions through macrophage activation and consequently may stimulate the release of fibrogenic cytokines otherwise growth factors may directly bind to acemannan, promoting their stability and prolonging their stimulation of granulation tissue [19–21]. *Aloe vera* contains saponin, Aloe genin which had been reported for wound healing activity [22].

Aloe vera gel also prevents progressive dermal ischaemia caused by burns, frostbite, electrical injury and intra arterial drug abuse. It acts as an inhibitor of thromboxane A2, a mediator of progressive tissue damage [23].

Table 3: Some Pharmacological and therapeutic potentials of aloe

Pharmacological activity	Research Activity	References
Wound healing	Case of radiodermatitis healed with aloe gel	[155]
	Aloe gel mixed with mineral oil in the treatment of thermal burns and scalds	[156]
	Radiation-induced ulcers effectively treated with aloe	[157]
	Use of *Aloe vera* leaf in the treatment of third degree x-ray induced ulcers in rats	[158]
	Second degree thermal and radium burns treated with aloe	[159]
	The healing action of extracts of *Aloe vera* leaf on abrasions of human skin	[160]
	Aloe accelerated ulcer healing activity in rabbits and increased collagen deposition	[161]
	Aloe vera used in the treatment of thermal and irradiation burns in laboratory animals and humans	[95]
	Aloe high water content keeps the wound moist and increased epithelial cell migration to promote wound healing	[3]
	Accelerated healing in frostbite wounds with aloe	[162]
	Aloe gel having ability to reverse progressive necrosis in partially damaged tissue	[163]
	Antiprostaglandins and antithromboxanes effect of aloe against frostbite wounds	[99]
	Effects of aloe extracts on human normal and tumor cells *in vitro*	[24]
	Tissue survival effect of aloe against frostbite wounds	[100]
	Topical effect of Aloe with ribonucleic acid and vitamin C on adjuvant arthritis	[164]
	Antiarthritic activity of anthraquinones found in Aloe for podiatric medicine; Wound healing and anti-inflammatory activity of *Aloe vera*.	[36, 165]
	Mannose-6-phosphate stimulate fibroblast to increase collagen and proteoglycan synthesis and increases wound tensile strength	[166]
	Aloe treated animals reduced five times edema response as compared to untreated diabetic group	[69]
	Eicosandoids and terpenes actively decreased inflammation in wounds; Wound healing. oral and topical activity of *Aloe vera*	[167]
	Plant hormones gibberellin and auxin stimulate antibody production and wound healing in a dose-response manner against gelatin induced inflammation	[70]
	Gel inhibits Thromboxane A2 synthetase and prevent its production to maintain a balance equilibrium between PGE2 and PGF2A	[168]
	The stimulation of post-dermabrasion wound healing with stabilized *Aloe vera* gel-polyethylene oxide dressing	[169]
	Aloe gel stimulates macrophages and fibroblasts through the binding of mannose 6-phosphate, which increase collagen and proteoglycan production for healing wound	[4]
	Beneficial effects of Aloe in wound healing	[98]
	Anti-inflammatory and wound healing activity of a growth substance in Aloe vera	[17]
	Wound healing effects of Aloe gel and other topical antibacterial agents on rat skin	[170]
	Wound healing potential of *A. vera* leaf gel studied in experimental rabbits	[171]
	Simultaneous application of *Aloe vera* gel and microcurrent treatment showed synergistical effect on open wounds	[172]

Continued

Table 3: *Continued*

Pharmacological activity	Research Activity	References
Anti-inflammatory	Aloe having anti-thromboxane properties, which dilate arteries and enhance local blood flow to treat inflammation	[32]
	Aloe extract showed bradykinase activity and Anti inflammatory properties	[30]
	Carboxypeptidase from aloe inactivate bradykinin to inhibits inflammation	[173]
	Emolin, barbaloin and emodin from aloe gel shows antithromboxane effect to maintain cellular integrity	[174]
	Mannose inhibits the human neutrophils oxidative burst and prevent tissue damage	[175]
	Anti-inflammatory activity of *Aloe vera* against a spectrum of irritants	[176]
	Aloe vera as a biologically active vehicle for hydrocortisone acetate	[38]
	Anti-inflammatory activity of *Aloe vera* gel due to arachidonic acid pathway via cyclooxygenase inhibition	[26]
	Anti-inflammatory activity of *Aloe* gel against croton oil induced mouse ear inflammation	[27]
	Cinnamic acid ester of aloesin extracted from *A. barbadensis* leaves shown to reduce croton oil-induced inflammation	[28]
	Mannose-6-phosphate shown to have anti-inflammatory activity like acetylated mannan, a gel component	[29]
	Lupeol, found in *Aloe vera*, contributed anti-inflammatory activity	[17]
	Anti-inflammatory and antipruritic effects of *Aloe vera* gel appears to exert through bradykinase activity, thromboxane B2, prostaglandin F2 inhibition and magnesium lactate respectively	[4, 31, 32]
	Prostaglandin E2 production inhibited by glycoprotein component of the gel, Aloctin A	[33]
	Veracylglucan B and Veracylglucan C (Maloyl glucan compound) isolated from aloe gel showed potent anti-inflammatory activities	[34]
	Aloin and aloe-emodin suppressed the inflammatory responses by blocking iNOS and COX-2 mRNA expression	[35]
	Decolorized aloe gel (anthraquinone-free gel) is more potent as an anti-inflammatory agent than the colorized (anthraquinone) form	[36]
	Hydrocortisone inhibited the inflammatory process in an additive, dose-dependent manner when given concurrently	[37, 38]
Immunomodulatory action	Stimulation of nitric oxide production in chicken macrophages	[21]
	Acemannan directly stimulated immunity through potentiating of lymphocyte response to alloantigen; activation of nitric oxide production by macrophages and cytokines (IL-1, 6, IFN, TNF)	[21,39]
	Enhancement of phagocytosis; and increment of circulating monocytes and macrophages	[40]
	A high molecular weight polysaccharide aloeride activate nuclear factor (NF-κB) in human macrophages and also induces the expression of the mRNAs.	[41, 42]
	Acemannan immunostimulant prevented ultraviolet (UV) irradiation-induced immune suppression in mice	[44]
	A mannose-rich polysaccharide fraction of aloe gel enhanced antibody production in mice.	[45]

Continued

Table 3: *Continued*

Pharmacological activity	Research Activity	References
Anti-cancer	Acemannan amplified antibody dependent cellular cytotoxicity and stimulated the propagation of thymic cells, also effective in the treatment of fibrosarcoma in dogs, cat and mice increased survival rate	[46–49]
	Potent anti-genotoxic and antitumor promoting activities of polysaccharides from *A. barbadensis*	[51]
	Acemannan stimulated the production of tumor necrosis factor (TNF), interleukin-1 and interferon by macrophages and showed antitumor effect	[39]
	Large doses of polysaccharides with squalene, vitamins A and E demonstrated chemopreventive and curative properties against mouse skin tumors	[52]
	Aloctins showed mitogenic activity for lymphocytes, binding of human 22-macroglobulin and also inhibits growth of methylcholanthrene-induced fibrosarcoma	[42, 53]
	Anthraquinone derivative Aloe-emodin is active against P-388 leukemia in mice	[54]
	Aloe-emodin showed favourable therapeutic index against neuroectodermal tumors	[56]
	Aloe-emodin had stimulatory effect on urokinase secretion and colorectal carcinoma cell growth	[57]
	Antimetastatic activity of aloe gel reported in experimental rats and mice by decreasing TXA2 and TXB2 production	[58, 59]
	Aloe gel demonstrated antiangiogenic activity in the synovial pouch model in mice	[60]
	Aloe extract had inhibitory effect against preneoplastic hepatocellularlesions in rats; A deterioration of the pleural tumor in rats by aloe latex, had also been demonstrated	[61–63]
	Simultaneous administration of aloe and melatonin enhances the remedial result against lung, gastrointestinal, and breast cancer by increasing interleukin-2 activity	[64]
	Aloe latex enhances the activity of 6-fluorouracil and cyclophosphamide	[47]

Several other mechanisms including polysaccharides induced complement stimulation, hydration, insulating properties of the gel have already been reported. *In vitro* studies demonstrated that the growth of normal human cells and attachment were promoted by exposure to fresh *Aloe vera* gel, whereas a stabilized gel was show to be cytotoxic to both normal and tumour cells and the cytotoxic effects were thought to be due to the addition of external substances to the gel during processing [24]. An increment in glycosaminoglycan components of the extracellular matrix, hyaluronic acid and dermatan sulphate levels had been observed over oral and topical application of *Aloe vera* on dermal wounds [25].

6.2 Anti-inflammatory Activity

The anti-inflammatory activity of *Aloe vera* gel has been revealed by a number of inflammatory models like kaolin, carrageenan, albumin, gelatin, mustard and croton oil which were said to act either by promoting prostaglandin synthesis or by increasing infiltration of leucocytes. *Aloe vera* gel has antiinflammatory activity and suggested its inhibitory action on the arachidonic acid pathway via cyclooxygenase [26]. Croton oil induced mouse ear inflammation was reduced by up to 67% through topically applied Aloe gel [27]. Similarly a component, cinnamic acid ester of Aloesin extracted from whole *Aloe barbadensis* leaves and probably originating from the exudates rather than the gel shown to reduce croton oil-induced inflammation [28]. Mannose-6-phosphate was shown to have anti-inflammatory activity like acetylated mannan, a gel component [18]. Acute inflammation induced by carrageenin was significantly reduced by fresh *Aloe vera* gel, although no effect was observed on chronic inflammation [29]. Specific plant sterols Lupeol, found in *Aloe vera*, also contribute to the anti-inflammatory activity in a dose dependent manner Anti-inflammatory and antipruritic effects of *Aloe vera* gel appears to exert through bradykinase activity [18,

30], thromboxane B2, prostaglandin F2 inhibition and magnesium lactate respectively [31, 32]. Prostaglandin E2 production also inhibited by glycoprotein component of the gel, Aloctin A [33]. From *in vitro* study it was confirmed that veracylglucan B and veracylglucan C (Maloyl glucan compound) isolated from Aloe gel have potent anti-inflammatory activities [34]. Aloin and Aloe emodin possibly suppress the inflammatory responses by blocking iNOS and COX-2 mRNA expression [35]. Aloe gel containing anthraquinone (colorized gel) and anthraquinone-free gel (decolorized gel) found that the decolorized Aloe gel is more potent as an anti-inflammatory agent than the colorized form [36]. The same authors also reported that PMN leukocyte infiltration and inflammation are decreased by both colourised and decolourised gel. Therefore on skin ailment management the role of anthraquinones is still confused and further studies are required to clarify the capacity of Aloe gel (acemannan) to interact with integrins, heterodimeric cell surface receptors. Integrins play a role in inflammation, permitting inflammatory cells to leave the bloodstream and enter damaged tissues [37]. Lastly, Aloe gel and hydrocortisone seem to inhibit the inflammatory process in an additive, dose-dependent manner when given concurrently [38].

6.3 Immunomodulatory Action

Acemannan can directly stimulate immunity through potentiation of lymphocyte response to alloantigen; activation of nitric oxide production by macrophages and cytokines (IL-1, 6, IFN, TNF) [39, 21]; enhancement of phagocytosis; and increment of circulating monocytes and macrophages [40]. A high molecular weight polysaccharide Aloeride contains glucose, galactose, mannose and arabinose and it can activate nuclear factor (NF-κB) in human macrophages as like as bacterial endotoxin, also induces the expression of the mRNAs encoding IL (interleukin)-1 and TNF (tumor necrosis factor)-α to levels equal to those observed in cells maximally activated by bacterial endotoxin [41]. Aloe gel also causes a local activation of complement at the level of C3 [42]. Commercially available acemannan immunostimulant is a partially purified carbohydrate preparation containing about 60% acetylated mannan with other carbohydrates, especially pectins and hemicelluloses prevent UltraViolet (UV) irradiation-induced immune suppression as determined by contact hypersensitivity response in mice [43]. MAP also inhibits UV irradiation-induced TNF (Tumor Necrosis Factor) release from human epidermoid carcinoma cells. All these results indicate that MAP can be used to reduce the risk of sunlight-related human skin cancer. Aloe extracts materialize to manipulate lymphocyte function under some circumstances, viz., prevent supp-ression of contact hypersensitivity and Delayed-Type Hypersensitivity (DTH) responses in mice by UltraViolet (UV) irradiation [44]. A mannose-rich polysaccharide fraction of Aloe gel has been shown in mice, to enhance antibody production [45].

6.4 Cancer

Acemannan is capable to amplify antibody dependent cellular cytotoxicity and stimulate the propagation of thymic cells, also effective in the treatment of fibrosarcoma in dogs, cat and mice increased survival rate [46–50). Lentinus edulis and others (Ganoderma lucidum, Coriolus versicolor) have demonstrated that polysaccharides from Aloe barbadensis have potent anti-genotoxic and antitumor promoting activities [51]. The antitumor effect of acemannan may be due to stimulation of the production of Tumor Necrosis Factor (TNF), interleukin-1 and interferon by macrophages; acemannan is also able to abrogate viral infections in both animals and men [39]. From the few reports available, it materializes that to produce immunostimulation and antitumor effects large doses of polysaccharides are necessary to with other substances like squalene, vitamins A and E have been demonstrated to have chemopreventive and curative properties in the prevention and treatment of mouse skin tumors and found to reduce the severity of chemical hepatocarcinogenesis in rats [52]. Aloe extract also contains aloctins, substances which possess many biological activities such as mitogenic activity for lymphocytes, binding of human 22-macroglobulin, complement activation via the alternative pathway and also inhibits growth of methylcholanthrene-induced fibrosarcoma and the results have been attributed to the immunomodulatory effect of aloctin A, not to its cytotoxicity [42, 53]. Anthraquinone derivative Aloe-emodin is active against P-388 leukemia in mice [54] and selective inhibitor of human neuroectodermal

tumor cell growth in tissue cultures and in animal models, the cytotoxicity mechanism consists of the induction of apoptosis, while the selectivity against neuroectodermal tumor cells is due to a specific energy-dependent pathway [55]. Aloe-emodin is lethal against neuroectodermal tumors with no substantiation of acute or chronic toxicity and as a result it shows a favourable therapeutic index. Aloe-emodin does not have inhibitory activity on the proliferation of normal fibroblasts or hemopoietic progenitor cells. However, others have examined Aloe-emodin as a cytotoxic agent on numerous tumor cell lines but no considerable activity was found [56]. A stimulatory effect of Aloe-emodin on urokinase secretion and colorectal carcinoma cell growth has also been described [57]. Diethylhexylphthalate (DEHP), isolated from *Aloe vera* was exhibited to have a potent antileukaemic effect in human cells and anti-mutagenic activity in the Salmonella mutation assay. The presence of all these compounds might be sufficient to clarify the prophylactic and probable therapeutic effect of Aloe extract and its antitumour activity against leucopenia caused by exposure to cobalt 60, sarcoma-180 and Elhrich ascites [58, 59]. Antimetastatic activity of Aloe gel has also been reported in Experimental rats and mice [47] and inhibits metastasis by decreasing TXA2 and TXB2 production in vitro [14] and this could be one of the mechanisms of antimetastatic activity of Aloe. Tumors endorse platelet aggregation by stimulating the production of TXA2 and/or inhibiting the production of PGI2. The importance of platelet aggregation in metastasis is now more widely accepted and several reports have been found that by modifying the balance between Prostacyclin (PGI2) (inhibits platelet aggregation) and Thromboxane (TXA2) (enhances aggregation) migrating cells from some cancers induce platelet aggregation. Glycoproteins isolated from Aloe arborescens and Aloe saponaria degrade bradykinin in vitro and inhibit the formation of histamine in vitro. Antiangiogenic activity of Aloe gel has also been demonstrated *in vivo* in the synovial pouch model in mice [60]. Other studies like, Aloe extract to have an inhibitory effect when used against preneoplastic hepatocellularlesions in rats, a deterioration of the pleural tumor in rats by Aloe latex, ability to augment tumor specific immunity etc. had also been demonstrated [61–63]. Clinical study had shown that patients with advanced solid tumors such as lung cancer, gastrointestinal cancer, breast cancer or brain glioblastoma, simultaneous administration of Aloe and melatonin enhances the remedial result through increasing interleukin-2 activity [64]. It has also been demonstrated that Aloe latex enhances the activity of 6-fluorouracil and cyclophosphamide [47]. Nevertheless, until well-designed clinical trials on Aloe are conducted, it will not be probable to determine the anticancer activity of the drug with certainty.

6.5 Diabetes

Even though preliminary clinical and experimental hypoglycaemic action had been reported in humans [65] earlier than animal (mouse) model of diabetes but, the mechanism of action for this effect has yet to be determined and it has been hypothesised that Aloe may stimulate the release or synthesis of insulin from the β-cell of Islets of Langerhans [66]. Another study have demonstrated that a formula containing *Aloe vera* and a small number of natural agents (*Nigella sativa* L., *Boswella carterii* Birdw., *Commiphora myrrha* Engl. and *Ferula assa-foetida* L.) inhibits gluconeogenesis and lowers blood sugar in an animal model [67]; but, it was found to be ineffective in lowering blood glucose levels of alloxan-treated rats [68]. A 'bitter principle' separated from crystalline (sic) Aloe produced significant lowering of fasting blood glucose levels when injected into alloxantreated mice [66]. Subcutaneous injection of *Aloe vera* gel preparation promoted diabetic wound healing, reduced abnormal sensitivity and oedema induced by mustard [69]. In a subsequent study, surprisingly, both *Aloe vera* gel and gibberellic acid were reported to have almost equal inflammation-reducing properties in chemically induced diabetic mice [70]. Clinical trials suggest that oral administration of Aloe gel might be a useful appendage for lowering blood glucose in patients with diabetes [71]. They have divided 72 women into two groups received one tablespoon of Aloe gel or placebo for 42 days. Blood glucose levels consequently decreased from 250 mg to 141 mg in the experimental group, while controls showed no significant changes. Except triglyceride levels, which fell significantly in the actively treated group, other variables like cholesterol, weight and appetite were remain unaltered in both groups. This study was neither randomized nor blinded

to patient or investigators. Bunyapraphatsara et al., [72] investigated the effects of Aloe gel in combination with a standard oral antidiabetic glibenclamide 5 mg, twice daily. In addition, for the period of the trial (42 days) they were given either placebo or Aloe gel as above. The results show similar decreases in blood glucose and serum triglyceride levels in the actively treated group, as described in the first trial.

6.6 Viral Diseases

Anthraquinone derivatives were found to inhibit several viruses in vitro, including herpes simplex of type 1 and type 2, pseudo-rabies, varicella-zoster and influenza [73]. Acemannan had been reported in vitro to have anti-HIV/AIDS activity through amplify the production and function of cytotoxic T cells in a dose-dependent manner [74]. Acemannan in combination with the antiviral agent Azidothymidine (AZT) and acyclovir protected the cells from rapid HIV-1 replication induced premature cell death. Antiviral activity of acemannan is due to inhibition of glycosylation of viral glycoproteins [75]. Consequently, Aloe extract has been considered as a probable therapy for AIDS, alone or in association with other antiviral drug to reduce the dosage and side-effects of antiviral treatment up to 90% [76]. Dianthrones and other anthraquinone derivatives like rhein and emodin have antiviral activity against human cytomegalovirus but, due to their low bioavailability systemic antiviral effects are less. Two randomized clinical trials, conducted by the same research group [77, 78] indicate that topical application of *Aloe vera* might be effective against the first episodes of genital herpes. In the first study they divided 120 patients into three parallel groups treated with placebo, Aloe gel or Aloe cream three times daily for two weeks. In case of placebo cream the numbers of cured patients were 7.5%, Aloe gel 45% and Aloe cream 70%. In addition, Aloe cream showed a shorter mean duration (4.8 days) of healing than Aloe gel (7 days) and placebo (14 days). Among 49 patients healed at the end of this trial period, 6 patient got relapse after 21 months of follow-up. In the second study, 60 patients were indiscriminately divided into two groups treated with placebo ceam and Aloe gel respectively had both significantly shorter healing time (4.9 days) and a higher number of cured patients (66.7%) compared with the placebo group. Three patients among 22 healed patients showed recurrence after 15 months.

6.7 Antibacterial Activity

Aloe gel (acemannan) had been reported to have antibacterial activity against *Staphylococcus aureus, Streptococcus* species, *Klebsiella pneumoniae, Enterobacter cloacae, Citrobacter* species, *Serratia marcescens*, *Pseudomonas aeruginosa* and other bacteria's [79]. Aloe gel also speed up the rate of healing, decreases the synthesis of prostanoids and inhibits infection by *Pseudomonas aeruginosa.*

6.8 Psoriasis

Anthrones have long been used as antipsoriatic agents but, their mode of action is not known exactly, although many biological molecules and receptors have been identified as potential targets of anthrones. The antipsoriatic activity of anthrones is probably due to; inhibition of O_2 utilization by cells, a reduction in size of the intracellular spaces, decrease in ribosomes and mitochondria, interaction with DNA, inhibition of various enzyme associated with cell proliferation and inflammation, interfear with redox reaction resulting in mitochondrial damage, destruction of membrane lipids in the psoriatic epidermis etc. had all been noted [80–84]. A clinical trial performed randomly among 60 patients with mild to moderate chronic psoriasis treated either an Aloe gel or placebo cream was self-applied three times per day for four weeks subsequently followed up to 12 months [85]. The cure rate in the Aloe gel group was 83% and only 7% in the placebo group.

6.9 Hyperlipidaemia

Nassif et al., [86] worked with 60 hyperlipidaemia patients who had not responded to dietary intervention, received either 10 ml or 20 ml Aloe gel or placebo daily for a period of 12 weeks. Blood lipid levels were measured before and after treatment for 4, 8 and 12 weeks. Total serum cholesterol was decreased by 15.4% and 15.5%, triglycerides by 25.2% and 31.9%, LDL by 18.9% and 18.2%, respectively, in the two groups receiving different doses of Aloe gel. In a small trial with monkey it was found that orall administration of Aloe gel lowered total

cholesterol by 61% and also increased proportion in the high density lipoprotein (HDL) [87].

6.10 Miscellaneous

Afzal et al., [88] stated that effect of Aloe extract may be due to the formation of some prostanoids throughout dark storage at 4°C–30°C, for a period of three to ten days. A study carried out with a formulation containing Aloe, silicon dioxide and allantoin to treat aphthous stomatites indicated that Aloe gel is less effective on aphthous ulcers but, bioadhesive patch prepared with Aloe gel is usefulness for the treatment of mouth ulcers has recently been evaluated and the results of this research emphasize the efficiency and acquiescence of the patch for the treatment of the aphtous stomatitis [89]. Antiparasitic actions of aqueous extract of Aloe barbadensis against in vitro culture of *Trichonomas vaginalis*, suggesting its growth inhibitory activity over *T. vaginalis* and its potential use in womens' disturbances [90]. Studies have also been showed that topical and oral use of Aloe formulation able to heal the patients with chronic venous leg ulcers [13]. It was found that growth rate of urinary calcium crystals that contribute to the deposition of kidney stones also reduced by Aloe [91]. Aloe is considered as a 'panacea' in veterinary medicine as a purge for cattle and in the treatment of different types of inflammation like ringworm, allergies, abscesses, fungal infections, thermal burns in dogs [92–94]. However, in the lack of better researchs we must be cautious against simplifications of these therapeutic treatments.

7. Clinical Studies

7.1 Anti-inflammatory and Wound Healing

To prove the effectiveness of Aloe gel and its various components to some sort of deliberate wounding or on inflammation a number of tests have been used. These require to be famed as of clinical trials where the injuries already exist and are comparatively treated scientifically by means of presumed therapeutic agents. Ashley et al., [95] first perform the most comprehensive and precise clinical trials with Aloe gel against controlled thermal and radiation burns on rats and rabbits compared with clinical studies on human patients. Goff and Levenstein, [96] was determine the tensile strength of the healing of a precise incision wound, post mortem. Clinical trial with humans, 68% of the Aloe-treated patients recovered fully and among them 7% required amputation, whereas only 33% of patientsa getting other treatments were fully healed [97]. A series of experiments of Aloe gel on heat burns, electrical burns and frostbite in guinea pigs, rabbits and in clinical studies with humans had been performed to demonstrate a therapeutic potential across the wide variety of soft tissue injuries and to recognize the possible multifarious activities of Aloe constituents [98]. Reduction of thromboxane levels was thought to be main function of Aloe gel in healing frostbite and depending on this hypothesis it had been used clinically to treat the more rigorous blisters where there was structural damage [99, 100]. In an inadequately described trial, Aloe was found to be less effective than silver sufladiazine cream in the treatment of experimental second degree burns, with an idea that Aloe may indeed disturb the healing process [101]. Schmidt et al., [102] observed the consequence of Aloe gel on the healing of 21 women undergoes complicated gynecological or obstetric surgical wounds. This study, was incision type and randomized to either standard treatment (debridement and irrigation), or standard treatment plus Aloe gel. Experimental group healed within 83 days on average versus 53 days with standard treatment ($P = 0.003$). Because of the clearly prolonged healing in the group treated with Aloe, patient recruitment was terminated before the desired sample size ($n = 114$) was reached. Another research, topical Aloe gel preparation versus Vaseline gauze on 27 patients with partial thickness skin burns, healing time was 12 days with Aloe gel treatment while 18 days with Vaseline gauze Visuthikosol et al., [103]. These contradictory results cannot be measured convincing, but must be considered. A small randomized placebo-controlled trial gave hopeful preliminary evidence over 44 individuals teated with oral *Aloe vera* gel (100 mL twice daily for 4 weeks) was advantageous in the supervision of ulcerative colitis [104]. Puvabanditsin et al., [105] carried out a double-blind, randomized, placebo-controlled study to review the usefulness of *Aloe vera* cream in prevention of burn and tan from ultraviolet light.

7.2 Constipation

Laxative action of aloin (1 grain [=0.0648 g] once) evaluated with phenolphtalein (2 grain once) and phenolphthalein (1 grain) + aloin (0.5 grain) and placebo over 28 healthy adults to different treatment sequences; stool frequency and transit time were compared for all treatments [106]. Odes & Madar, [107] performed a randomized double-blind placebo-controlled study and found that Aloe in combination with celandine and psyllium was an effectual laxative in patients suffering from chronic constipation.

7.3 Antiviral

Two non-randomized trials had been performed with oral acemannan in the treatment of HIV infection to prove the efficacy of Aloe gel and that had been published as conference abstracts [108, 109]. Montaner et al., [110] accomplished a randomized double-blind trial on antiretroviral agent for HIV to evaluate the effectiveness of acemannan as an adjuvant over 63 patients to receive either 400 mg oral acemannan four times daily or placebo. There was no significant divergence in CD4 counts, CD4/CD8 ratios, P_{24} antigen, β_2-microglobulin concentration, viral load between the two treatment groups etc. A randomized study was carried out with 60 men genital herpes patients receive topical Aloe consisted of three daily applications of a 0.5% cream for five days versus applications of a cream without active ingredients [98]. After one week of treatment 2/3 patients treated with Aloe were cured of wounds in the compared with only 2/30 in the placebo group ($P < 0.001$).

7.4 Cancer

Sakai, [111] carried out a trial over 192 subjects (1 case per 2 controls) in a multi-center Japanese case-control study to determine the potential correlations between lung cancer incidence, smoking, and consumption of 17 different types of plants.

7.5 Diabetes

Dried Aloe gel was studied in five patients with type 2 diabetes orally for half a teaspoon of Aloe daily for 4–14 weeks, after that fasting glucose level was measured to have fallen from a mean of 273 to 151 ($P < 0.05$) [65]. Two non-randomized clinical trials had been conducted to conclude that Aloe gel might have similler efficasy as a sulfonylurea antihyperglycemic oral agent, glibenclamide to lower blood glucose in type 2 diabetes mellitus [71, 112]. Chalaprawat, [113] performed a randomized double-blind placebo-controlled crossover trial and found no hypoglycemic effect of Aloe juice (15 mL twice daily) in 16 type 2 diabetics.

8. Adverse Effects, Toxicity, Drug Interaction and Safety Evaluation

Long term Aloe treatment about three to six months or more than that in rats suggest that does not induce tolerance in the sense of a reduced laxative effect. Evnthough, genotoxicity have already been shown by anthraquinone derivatives in *Salmonella* assay but, the clinical relevance of this experimental result is still not clear [83, 114–116]. Laxative use did not show any significant increase of colon cancer incidence [117–120]. Risk of colon cancer was found to inter-related between constipation and to use of anthraquinone laxatives but, epidemiological studies are in difference [121, 122]. Just similar to other laxative drugs such as senna, rhubarb, etc., which are digested by colon microflora, with Aloe latex abdominal discomfort, abdominal pain, meteorism, flatulence, cramps may be usual [123] and other side-effects comprise hemorrhoid congestion and coloration of the urine which becomes orange if the pH is acidic, or reddish purple if the pH is alkaline and this is due to the renal excretion of the hydroxyanthracene derivatives [124]. Prolonged use or overdosage may cause nephritis, vomiting, bloody diarrhoea with mucus or watery diarrhoea leading to electrolyte imbalance and hemorrhagic gastritis [125]. The increased intestinal loss of K+ can lead to hypokalemia, leading to further reduction of colonic motility while Na+ loss can result in secondary hyperaldosteronism ultimately may lead to fatigue, muscular weakness, weight loss, mental disturbances, steatorrhoea, electrocardiographic abnormalities kidney dysfunction, surface epithelium may damage and also may impaire the function of autonomic nervous system [126, 127]. Hypokalemia, which results from K+ loss, may produce agonistic action over digoxin, and thiazide diuretics, corticosteroids and licorice may aggravate hypokalemia [128]. These changes, however,

have not been clearly demonstrated in animals and humans. The morphological basis of pigmentation is melanosis (melanin synthesis), within macrophages of the large intestinal mucosa. An association between the laxative administration and melanosis is now been accepted but there is no indication that melanosis has any pathophysiological consequences. Once the laxative administration has stopped the intestinal mucosa recovers its usual coloration 4–12 months [124]. Jacobs and White [129] reported that when the colon cancer risks for constipation and laxatives were adjusted for each other, the association with laxatives disappeared, whereas the association with constipation remained strong. Furthermore, when Aloe was administered with a carcinogen agent Azoxymethane (AOM), did not create any significant increase of ACF, and tumors. These results are basically in concurrence with earlier reports on other anthraquinone drugs [130, 131]. Studies have also been demonstrated that anthraquinone compounds like emodin selectively blocks the signal transduction modulated by oncogene through the inhibition of protein kinase and this hypothesis suggests ample edge of safety for Aloe and other anthraquinone drugs when used internally [127]. Aloe gel has been reported to cause contact and photo dermatitis or erythema with papulous when applied topically, in spite of its wound-healing and anti-inflammatory properties [117, 118, 132–137). It was found that on exposure to ultraviolet radiation Aloe emodin painting on the skin of mice results in the progression of melatonin-containing skin tumors [138]. Boon and Smith, [124] reported one case of cathartic effect after topical application of Aloe gel. Ten controlled clinical trials had been performed with 803 subjects did not show any withdrawals or serious adverse reactions, some patients experienced burning after topical application, contact dermatitis and mild itching. All adverse effects were reversible and *Aloe vera* was generally well tolerated [139]. Scientific evidence for the cosmetic and therapeutic effectiveness of *Aloe vera* is limited and when present is typically contradictory. Despite this, the cosmetic and alternative medicine industries regularly make claims regarding the soothing, moisturizing and healing properties of *Aloe vera*. It is common practice for cosmetic companies to add sap or other derivatives from *Aloe vera* to products such as makeup, tissues, moisturizers, soaps, sunscreens, incense, razors and shampoos. However, the species is used widely in the traditional herbal medicine of China, Japan, Russia, South Africa, the United States, Jamaica and India. Research studies highlight the tremendous healing powers of Aloe when used both internally and externally.

9. Gel Preparation Factors Influencing over Processing of Gel

It would appear that several contradictory clinical results acquired for therapeutic efficacy of Aloe gel result from the history of the sample after removal from the leaf, or even growing conditions of the plant. This was reviewed and allegedly concluded in a report from the United Aloe Technologists Association [140, 141]. High Temperatures for Short Times (HTST) method is usefull throughout pasteurization is one of the stresses obligatory on the gel and there are advantages in using preferably with the incorporation of an antioxidant such as ascorbic acid [142]. Mucopolysaccharide veracity upon storage was found to be conserved by the addition of other natural polysaccharides which act synergistically [143–145]. Size exclusion chromatography is usefull for number of commercial 'Aloe' products exposed extensively differing levels of mucopolysaccharides [146]. Organoleptic properties are important when the gel is intended for internal use, for those cses these processes are also important where and additives must be carefully chosen [147]. It was also alleged that plants grown hydroponically had higher carbohydrate content [148]. There are still other factors like leaf size, pH, fiber content, calcium and magnesium contents and certain HPLC peaks operating since a cautious analysis of plants from many geneses showed great variation [149]. Lastly anthraquinone derivatives ('aloin') derived from the mesophyll exudate is one of the problem. Protocols to address all these troubles are now been stabilized and set out in detail in two US Patents [150, 151].

10. Current Market Scenario and Export Potential

The current global turnover of raw Aloe leaves amount up to 70–80 million US dollars, which is expected to grow at the rate of 35% in the next five years. For

processed derivatives and value added products, current global trade is estimated at around 1 billion and 25 billions US dollars respectively. USA supplies the major bulk of Aloe in world market having a share of 60–65%, whereas Latin American countries supply 20–25% and Australia, China and India combined together have a market share of only 10%. American consumers are most familiar with Aloe's use in skin-care products and there have been dramatic increases in *Aloe vera* sales in the United States. As a beverage, Aloe drinks have long been a staple drink in American health food stores and with direct marketing companies. Korea is currently the largest international market place for Aloe, with Japan running a close second. Both of these countries have a long and respected tradition of herbal medicine. Aloe beverages are also very popular in Korea, Singapore and Malaysia. In Australia, market for skin and hair products containing Aloe is increasing. The use of Aloe in cosmetic products is growing at a modest rate in the Scandinavian countries, Switzerland, Italy, Spain and in several African nations. Aloe produced in Zanzibar, West Indies, Cape Colone, Bonaire, etc, is shipped to the United States and Europe. In India, Aloe juice produced at the farms in Vidharbha region is marketed to Mumbai and Bangalore.

11. Discussion

Herbal medicines derived from plant are part of this system since ancient human civilizations and very prominent to the rural areas where the 65% of population live. The ethnic and rural people of India have preserved a large bulk of traditional knowledge of medicinal uses of plants growing around them. As to execute the requirement of medicinal plants, it becomes essential to promote these plants species for cultivation. According to a WHO estimate, globally about 80% of the population relies on traditional medicine. Beside these, thousands of other phyto molecules with therapeutic potentials using by rural and tribal's but has not been standardized till date require more sophisticated techniques for rapid investigations. Therefore for past two decades, renewed interest in health products through herbal medicine globally has opened new avenue of exploration and they impart debate. *Aloe vera* has been used since ancient times for many healing and beauty purposes. It has been the issue of growing technique, scientifically based investigations for wide range of possible curative and healing effect apart from what is already in practice around the world. Various research studies are in pipeline to discover the potential of *Aloe vera* such as boosting immunity, treatment against HIV virus, managing diabetes along with treat certain types of cancer. Public interest is Aloe has grown quickly, and now there is a considerable amount of research into the various components of Aloe to find our more about their properties and to characterize these components so that more specific research can provide clues to the "magic" that is attributed to *Aloe vera*.

In India the whole Aloe plant has been used as a purgative, stomachic, antihelmintic and emmenagogue, menstrual suppression and the root for colic pain [152]. Aloe has also been used for unrelated human illness like to correct kidney ailments, enhance sexual excitement, develop the mammary glands, relieve headaches, suppress fever in children, as a laxative and skin injuries [153]. Clinical trials are now in improvement to afford convincing evidence not only in these diseases but also in arthritis, gastric ulcer, cancer, AIDS and colitis.Aloe gel can be useful abundantly for topical applications, wide ranges of products are now available on the market; however, simply pure Aloe gel is sufficient to treat several skin disorders. These products are light and heat sensitive; therefore after removing the gel from leaf mechanically it is being preserved with buffer and stabilized immediately, this process may fluctuate from producer to producer, making the superiority of Aloe gel highly variable [125]. Aloe products are classified as drugs at the same time as dietary supplements, also a common ingredient in numerous hand, body and sun lotions, shaving creams, shampoos and personal care-products. This is why sometimes people forget to consider Aloe a medicinal drug [154]. Aloe is also processed into various flavoured and unflavoured alcoholic drinks that are ingested with the belief that this bitter liquid (amarum) will stimulate the appetite and/or the digestion. Many multi-level marketing companies are selling wide range of *Aloe vera* based health and beauty products. Many of these products are being sold in India. Keeping in view, the blooming stage of Indian herbal industry and export potential, commercial cultivation of *Aloe vera* can be very rewarding for Indian farmers.

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