

1 *Mini Review*

2 **Phytochemical and Pharmacological Properties of** 3 ***Chaenomeles Speciosa*: an Edible Medicinal Chinese** 4 **Mugua**

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18

19 **Abstract:** *Chaenomeles* plants are adapted to diverse ecological zones particularly the temperate areas of
20 Korea, Japan and China. In China, *Chaenomeles speciosa* mainly planted in Chongqing, Anhui and Hubei
21 provinces. Most of the studies till date have been focused on the anti-inflammatory activities of *C. speciosa*
22 fractions. The present study aimed to review the maximum literature reported for the presence of various
23 phytochemicals in *C. speciosa*. In addition, the pharmacological properties of these chemical compounds of
24 this plant shall also be discussed. The extracts of the various parts of the plant are rich in diversity of
25 antioxidants, organic acids, phenolics, terpenoides and many different phytochemicals that bear strong
26 anticancer, antioxidant, anti-viral, antibacterial properties, anti-inflammation, anti-hyperlipidemic,
27 anti-hyperglycemic and anti-parkinson properties. *C. speciosa* fruits have broad scope in industry as well as
28 in medicines. Not only the leaves and fruits of *C. speciosa* plant, but various other parts including roots, seeds,
29 bark twigs, and flowers all have long history of clinical trials in curing many human ailments. However, the
30 maximum accessible data concerning the chemical composition and their broad pharmacological properties of
31 *C. speciosa* plant parts is pretty restricted that make it more appealing for indepth investigations.

32 **Keywords:** *Chaenomeles speciosa*, TCM, antioxidants, phytochemicals, anti-inflammation

33

34 **1. Introduction**

35 *Chaenomeles* plants are adapted to diverse ecological zones, but mostly occupied the temperate areas of
36 Korea, Japan and China. In China, It is mainly planted in Chongqing, Anhui and Hubei provinces, and locally
37 called ‘Zhoupi mugua’, which has been well documented in broad traditional Chinese herbal medication
38 systems. Recent scientific studies unveil high nutritional value of this plant. In the past few decades,
39 cultivation of *C. speciosa* became a part of routine agriculture and fulfilling an ever increasing demands of the
40 industry particularly the fruits juices, fruits tea, vinegar and fruit preservation etc. Many of the agriculture
41 varieties has been introduced in the market, to increase the gross yield of which three traditional varieties are
42 well known i.e., Luohanji, Zimugua and Changjun [1]. The extracts of the fruits of *C. speciosa* are rich in
43 diverse antioxidants and many different phytochemicals that bear strong anti-cancer, antioxidant, anti-viral,
44 antibacterial properties, anti-inflammation, anti-hyperlipidemic, anti-hyperglycemic and anti-parkinson
45 properties [2-6].

46 *Chaenomeles* are enriched with antioxidants and α -glucosidase inhibitory activities are well documented
47 in recent studies [7]. Various parts of the *Chaenomeles* plant have variable amounts of phytochemicals such
48 as peels are rich in triterpenes due to which its highly antioxidant [7]. This is quiet common observation
49 which is being supported by multiple studies, that peels of a variety of fruits such as pear and hawthorn are
50 having more antioxidants [8]. In case of *Chaenomeles* most of its peels are being wasted and ultimately huge

51 amount of good source of antioxidants is gone wasted [8], hence *Chaenomeles* is a potential candidate in
 52 terms of superior performance due to its higher α -glucosidase and antioxidant functions [7]. In addition to
 53 these, various triterpenes and phenolics are also present in the plant extracts, especially ursolic and oleanolic
 54 acids which are potential chemicals being recognized even in People's Republic of China Pharmacopoeia.
 55 Moreover, various minor but active compounds *viz.* chlorogenic acid, catechin, epicatechin, gallic acid,
 56 protocatechuic acid, caffeic acid and syringic acid have also been isolated from *Chaenomeles* [9, 10]. *C.*
 57 *speciosa* fruits are well studied for their ingredients and phytochemical compounds such as polyphenols and
 58 vitamin C [11], and studies depicted that it could be a good source for the natural antioxidants and sufficient
 59 amount of fibers and low amount of citric acid [11, 12].

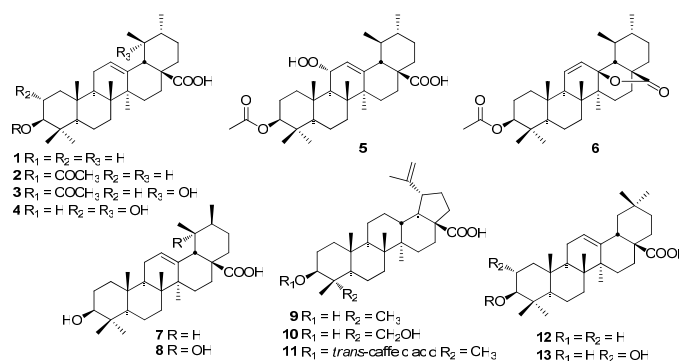
60 *C. speciosa* is a member of family Rosaceae, and also known as flowering quince [13]. Traditionally, *C.*
 61 *speciosa* has widely been used in clinical trials to treat hepatitis, rheumatoid arthritis and prosopalgia [14]. It
 62 is also used as an edible food, canned food, preserved fruit, fruit wine, fruit vinegar, and juices [13]. Most of
 63 the studies till date have been focused on the anti-inflammatory activities of *C. speciosa* fractions. The present
 64 study aimed to review the maximum literature reported for the presence of phytochemicals in *C. speciosa*. In
 65 addition, the pharmacological properties of these chemical compounds of this *Chaenomeles* fruits shall also
 66 be discussed.

67 2. Chemical Constituents

68 Up to now, approximately 64 chemical constituents have been isolated and identified from *C. speciosa*,
 69 including triterpenes, sesquiterpenoids, flavonoids, phenylpropanoids, phenols, biphenyls, and others. Among
 70 them, triterpenes and flavonoids were considered to be the primary bioactive constituents of *C. speciosa*. The
 71 components isolated from *C. speciosa* are summarized in the current review (Figures 1–7).

72 2.1. Triterpenes

73 Triterpenes are regarded as the major bioactive ingredients of *Chaenomeles* species, and phytochemical
 74 studies are focusing this genus since last two decades [15]. To date, 13 steroid compounds have been isolated
 75 and identified from *C. speciosa*. The steroids and their chemical structures are well described in recent studies
 76 (Table 1 and Figure 1). They all exist in the form of aglycones, that belong to pentacyclic triterpenoids,
 77 including ursanes (1-7), lupanes (8-11), and oleananes (12 and 13).



78
79 **Figure 1.** Chemical structures of triterpenes from *C. speciosa*.

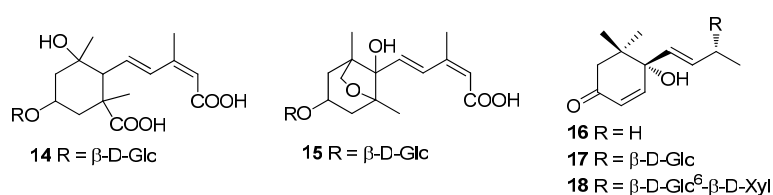
80 **Table 1.** Triterpene compounds from *C. speciosa*.

No.	Compounds	Parts	Ref.
1	ursolic acid	fruits	16-18
2	3-O-acetyl ursolic acid	fruits	16,17,19
3	3-O-acetyl pomolic acid	fruits	19,20
4	tormentic acid	fruits	16,17
5	speciosaperoxide	fruits	16,17
6	3 β -acetoxyurs-11-en-13 β ,28-olide	fruits	16,17

7	dihydrotomentosolic acid	twigs	21
8	ilexgenin B	twigs	21
9	betulinic acid	fruits, twigs	19-21
10	23-hydroxybetulinic acid	twigs	21
11	pycarenic acid	twigs	21
12	oleanolic acid	fruits	15-18,20,22
13	maslinic acid	fruits, twigs	16,17,21

81 2.2. Sesquiterpenoids

82 Sesquiterpenoids represent a relatively small group of compounds in *Chaenomeles* species. To date, only
83 five sesquiterpenoids were obtained from the ethanolic extract of *C. speciosa* so far. Their structures of these
84 compounds are shown in Table 2 and Figure 2.



85

86

Figure 2. Chemical structures of sesquiterpenoids from *C. speciosa*.

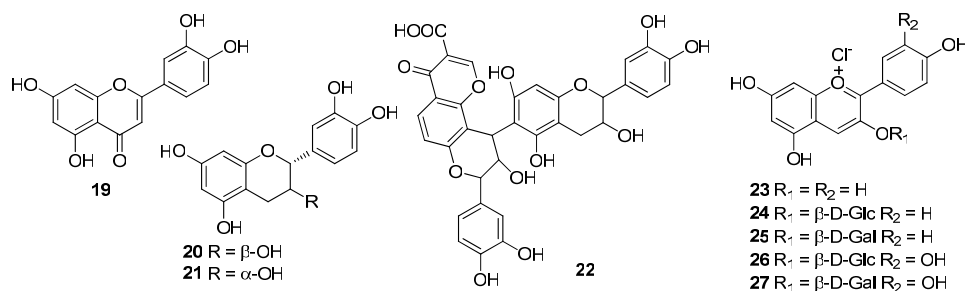
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Table 2. Sesquiterpenoid compounds from *C. speciosa*.

No.	Compounds	Parts	Ref.
14	speciosaoside A	fruits	23
15	(1'R,3'R,5'R,8'S)-epi-dihydrophaseic acid- β -D-glucoside	fruits	23
16	Vomifoliol	fruits	16,17
17	roseoside	fruits	16,17,24
18	(6S,7E,9R)-6,9-dihydroxy-4,7-megastigmadien-3-one 9-O-[β -D-xylopyranosyl(1 \rightarrow 6)-glucopyranoside]	fruits	16,17,24

88 2.3 Flavonoids

89 Flavonoids comprised of a huge number of polyphenolic compounds having a benzo- γ -pyrone
90 organization, which is universally occurred in plant kingdom; there is no exception for *Chaenomeles* species.
91 Flavonoids are the second major bioactive constituents in *Chaenomeles* species and their are divided into three
92 categories including one flavone (19), three flavanonols (20–22), and five anthocyanins (23–27). Their
93 structures of these compounds are shown in Table 3 and Figure 3.



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Figure 3. Chemical structures of flavonoids from *C. speciosa*.

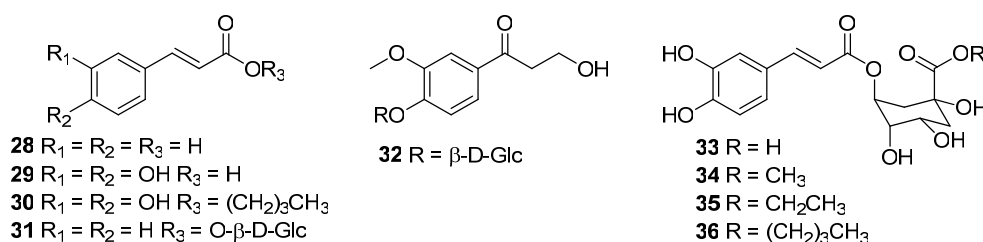
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Table 3. Flavonoid compounds from *C. speciosa*.

No.	Compounds	Parts	Ref.
19	quercetin	fruits	17,25
20	catechin	fruits	18
21	(-)-epicatechin	fruits	26
22	specpolyphenol A	fruits	27
23	pelargonidol chloride	petals	28
24	pelargonidin 3- <i>O</i> - β -D-glucopyranoside	petals	28
25	pelargonidin-3-galactoside	petals	28
26	cyanidin 3- β - <i>O</i> -glucoside	petals	28
27	cyanidin 3- <i>O</i> - β -galactopyranoside	petals	28

97 **2.4 Phenylpropanoids**

98 *Chaenomeles* species are also rich in phenylpropanoids. Almost 9 phenylpropanoids were isolated and
 99 identified from *C. speciosa* to date. These phenylpropanoids include 8 phenylpropionic acids (**28–31** and
 100 **33–36**) and one phenylpropanol (**32**). Their structures of these compounds are elaborated in Table 4 and
 101 Figure 4.



102

103

Figure 4. Chemical structures of phenylpropanoids from *C. speciosa*.

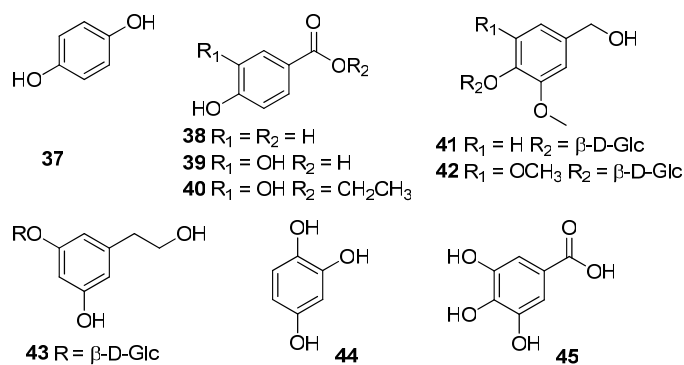
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Table 4. Phenylpropanoid compounds from *C. speciosa*.

No.	Compounds	Parts	Ref.
28	cinnamic acid	fruits	26
29	caffeic acid	fruits	22,26
30	n-butyl caffeate	fruits	22
31	1- <i>O</i> - <i>p</i> -coumaroyl- β -D-glucose	fruits	24
32	specphenoside A	fruits	27
33	chlorogenic acid	fruits	26
34	methyl chlorogenate	fruits	26
35	ethyl chlorogenate	fruits	20
36	5- <i>O</i> -caffeoylquinic acid butyl ester	fruits	26

105 **2.5 Phenols**

106 Many studies reported the presence of the aliphatic compounds in *Chaenomeles* species. Nine phenols
 107 (**37–45**) were isolated from *C. speciosa*. Their structures of these compounds are shown in Table 5 and Figure
 108 5.



109

110

Figure 5. Chemical structures of phenolics from *C. speciosa*.

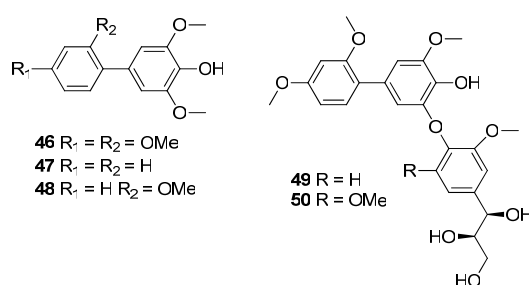
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Table 5. Phenolic compounds from *C. speciosa*.

No.	Compounds	Parts	Ref.
37	hydroquinone	fruits	25
38	4-hydroxybenzoic acid	twigs	21
39	3,4-dihydroxybenzoic acid	fruits	17,20,25,26
40	protocatechuic acid ethyl ester	fruits	26
41	vanilloloside	fruits	27
42	di- <i>O</i> -methylcrenatin	fruits	27
43	3,5-dihydroxyphenethyl alcohol 3- <i>O</i> - β -glucopyranoside	fruits	27
44	1,2,4-hydroxybenzene	fruits	24
45	gallic acid	fruits	20,24

112 2.6 Biphenyls

113 To date, only five biphenyls (**46–50**) were obtained from the ethanolic extract of *C. speciosa*. Their
 114 structures of these compounds are shown in Table 6 and Figure 6.



115

116

Figure 6. Chemical structures of biphenyls from *C. speciosa*.

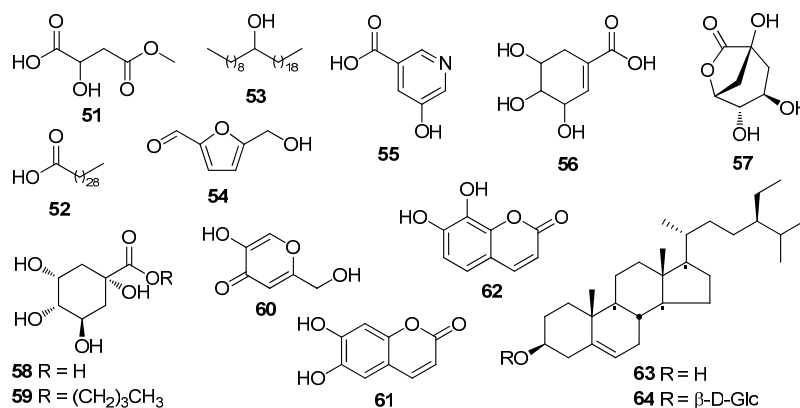
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Table 6. Biphenyls from *C. speciosa*.

No.	Compounds	Parts	Ref.
46	2',4'-dimethoxyaucuparin	twigs	21
47	aucuparin	twigs	21
48	2'-methoxyaucuparin	twigs	21
49	chaenomin B	twigs	21
50	chaenomin A	twigs	21

118 2.7 Others

119 In addition to the above mentioned main components, other components (Table 7 and Figure 7) are also
 120 found in *Chaenomeles species*, such as atty acid (51–53), quinic acids (57–59), coumarin (61 and 62), and
 121 steroids (63 and 64).



122

123

Figure 7. Chemical structures of other constituents from *C. speciosa*.

124

Table 7. Other compounds from *C. speciosa*.

No.	Compounds	Parts	Ref.
51	3-methyl-3-hydroxybutanedioic ester	fruits	17,25,29
52	triacontanoic acid	fruits	26
53	nonacosan-10-ol	fruits	15,18
54	5-hydroxymethyl-furan-2-carbaldehyde	fruits	26
55	5-hydroxynicotinic acid	fruits	24
56	shikimic acid	fruits	18
57	(-)-quinide	fruits	24
58	quinic acid	fruits	18
59	quinic acid butyl ester	fruits	26
60	kojic acid	fruits	20
61	esculetin	fruits	26
62	7,8-dihydroxycoumarin	fruits	26
63	β-sitosterol	fruits	15,18,22
64	daucoesterol	fruits	15,18,22

125 3. Pharmacological Activities

126 Various natural compounds have been served huge industrial and individual demands in curing multiple
127 diseases due to their potential pharmacological properties. This lust gained attention of the scientists to
128 continue exploration of such similar plants and compounds bearing similar medicinal importance. Dried
129 *Chaenomeles* fruits are being used as traditional herbal medicines since centuries within mainland of China to
130 cure dysentery, prosopalgia, rheumatoid arthritis, cholera, beriberi, vitamin C deficiency syndrome, enteritis
131 and hepatitis [14, 30]. Presence of complex compounds such as phenolics, tannins, multiple organic acids,
132 glycosides and flavones in *Chaenomeles* made it an important plant having diverse pharmacological
133 properties [31, 32]. Following sections will highlight and updates about the various pharmacological
134 properties of *Chaenomeles* plant reported in recent years. *Chaenomeles* plant has said to possess diverse
135 biological functions due to which its been in use since centuries in traditional Chinese medicine [13, 30, 33].
136 Modern day research also confirmed that *C. speciosa* is enriched in diverse pharmacological and biological
137 properties particularly anti-inflammation, immunomodulation, anti-microbial, anti-tumor and antioxidant
138 actions are notable [33, 34].

139 3.1 Anti-oxidant property

140 The botanical extracts are a potential source of natural antioxidants with almost no side effects [13]. The
141 extracts of *C. speciosa* fruits have very strong antioxidant ability. In a recent study, it was claimed that *C.*
142 *speciosa* have a strong potential for scavenging free radicals i.e., various reactive oxygen species (ROS) and
143 free nitrous oxide mainly due to the presence of strong antioxidant compound quercetin [17]. In
144 atherosclerosis, level of LDL increased with decreased antioxidant capability in the blood due to the
145 formation of LDL-oxidation complexes [35], which was successfully treated with the application of powdered
146 *C. speciosa* was thought due to its higher antioxidant nature of the plant parts that increased increasing the
147 anti-oxidant levels in the blood and declining the cholesterol levels [36]. Moreover, various polysaccharides
148 are being extracted from *C. speciosa* and reported to possess strong antioxidant activity [37].

149 A huge amount of flavonoid contents reported in *C. speciosa* has shown significant reduction in peroxide
150 levels in lard, remove DPPH and de-oxidized the iron (Fe^{3+}) in a concentration-dependent fashion,
151 demonstrating its strong antioxidant nature than ascorbic acid (vitamin C) [38]. Moreover, quercetin and
152 3,4-dihydroxybenzoic acid which were extracted from *C. speciosa* showed higher inhibition for DPPH
153 (2,2-diphenyl-1-picrylhydrazyl) and neuraminidase [17]. The antioxidants activity in five species of
154 *Chaenomeles* (*Mugua*) was studied and about 44 fractions were prepared that showed a potent and stable
155 free-radical DPPH and the hydroxyl radicals scavenging activity [39].

156 3.2 Anti-Inflammatory and analgesic activities

157 *C. speciosa* plant also being administered in inflammatory and immune related issues, and glucosides
158 present in the extracts have strong anti-inflammation as well as immunoregulatory properties [34, 40].
159 Methyl-3-hydroxybutanedioic ester found in *C. speciosa* has also been reported to possess strong
160 anti-inflammatory effects particularly in inflammatory avian influenza and dyspepsia [17]. Various plant
161 extracts even in fractions have also been reported to possess good potential against inflammations, pains and
162 anti-analgesic activity mainly due to the presence of chlorogenic acid [13]. Some of the *Chaenomeles*
163 polysaccharides also showed anti-inflammatory activities [41]. In another study, it was reported that
164 *Chaenomeles* fractions control the calcium channels, due to which it has got higher analgesic activity [42]. *C.*
165 *speciosa* plant is in use since long time to treat rheumatoid arthritis in various parts of China primarily due to its
166 anti-nociceptive and anti-inflammatory potential [40]

167 3.3 Anti-atherosclerotic effects

168 As arteriosclerosis is a systemic condition, hyperlipidemia, especially oxidized low-density lipoprotein
169 (LDL), are major elements that initiate this route and resulting in the formation of plaque [43].
170 Atherosclerosis is a condition, where the level of anti-oxidants decreased within the blood due to oxidation of
171 LDL. Level of LDL increased with decreased antioxidant capability in the blood due to the formation of
172 complexes [35], which was successfully treated by the application of powdered *C. speciosa*. It was thought

173 due to the higher antioxidant nature of the plant parts by increasing the antioxidant levels in the blood and
174 declining the cholesterol levels [36].

175 3.4 Anti-tumor and immunomodulatory activities

176 Cancer is the main cause of a large number of deaths across the world. Most of the cytotoxic drugs being
177 used to cure cancer tissues have also been reported harmful to the normal tissues [44]. An average molecular
178 weight water-soluble polysaccharide was successfully extracted from *C. speciosa* that is composed of glucose,
179 rhamnose, galactose, and andarabinose. This polysaccharide is good in inhibiting the tumor growth in the mice
180 along with improvement in delayed type hypersensitivity and higher secretion of interleukin (IL)-2, TNF- α and
181 IFN- γ in blood serum [45]. It is further suggested that the antitumor effects of this polysaccharide is might due
182 to the association with its potent immunostimulatory activity *in vivo* [45]. Many of the plant based
183 polysaccharides are less nontoxic with hardly any serious problems compared with certain synthetic compounds,
184 hence make these polysaccharides a superior choice for modern medication [46, 47].

185 Its was in the mid 1970s, when it was first time said that various organic acids present in *C. speciosa* have
186 strong antitumor activity studied on Ehrlich ascites carcinoma in mice [48], and this anti-tumor activity is
187 because of the presence of multiple terpenoids [49, 50]. Among various acids present in this plant includes
188 betulinic-, maslinic-, oleanolic- and ursolic-acids are the prominent triterpenoid chemicals [51]. Oleanolic and
189 ursolic acids in plants have inhibitory effects on estrogen receptor-negative breast cancer, osteosarcoma cells
190 and HuH7 human hepatocellular carcinoma cells, induce quick apoptosis in the cancer cells [51-53]. Moreover,
191 various acids present in the plant extracts including maslinic acids showed potential anti-angiogenic properties
192 on non-small-cell and lung cancer cells [51, 54]. *In vivo*, ethanolic extracts of *C. speciosa* checked the growth of
193 tumors along with increased immune responses in mice, while Foxp3, TGF- β and PD-L1 protein expression
194 levels were reduced within the tumors [3]. It was the pioneer study that explained ethanolic extracts of *C.*
195 *speciosa* strongly inhibited the growth and invasion of tumors by direct killing of cancerous cells as well as
196 enhanced immune responses [3].

197 3.5 Anti-diarrhea

198 Various organic acids (betulinic-, oleanolic-, and ursolic-acids) are the active components in fruits of *C.*
199 *speciosa* which are regarded as potent therapeutic candidates in treating LT-induced diarrhea [55]. Moreover,
200 studies used the extracts of *C. speciosa* showing strong antimicrobial activity and analgesic effects [13, 33]. It
201 is further suggested that G-protein-AC-cAMP regulated signaling have a major role in reducing the
202 inflammation and deterioration of joints in arthritis rats [40]. Intervention of intracellular signaling cascades
203 in synoviocytes by using glucosides of *C. speciosa* may consequently suppressed the deterioration of bones
204 and reduction of inflammations in autoimmune rat models. The major and prominent effect of *C. speciosa*
205 glucosides on higher cAMP levels in synoviocytes are thought to be linked with its inhibitory protein (Gi).
206 Moreover, this Gi-protein mediated AC-cAMP signaling cascade is thought to be one of the vital procedures
207 in reducing inflammations and modulating-immune responses by glucosides of *C. speciosa* [56-58].

208 3.6 α -glucosidase inhibitory

209 Among many varieties being cultivated within China, *C. speciosa* Var. Yunnan showed maximum
210 antioxidant potential along with α -glucosidase inhibition [59]. Moreover, another study confirmed that in *C.*
211 *speciosa* total amount of polysaccharides, flavonoids, ursolic acid and polyphenols are the prominent
212 phytochemicals bearing good antioxidant properties. In addition to it, complete polysaccharides and flavonoid
213 contents are mainly involved in inhibition of α -glucosidase activity of *C. speciosa* [60]. Such studies shall be
214 helpful in qualitative evaluation of the *C. speciosa* and its implementation in different industries. Moreover,
215 peels can be a good source of inhibitors of α -glucosidase activity and antioxidants within the broad range of
216 pharmaceutical as well as related industries [1]. Until now, many phytochemicals having strong α -glucosidase
217 inhibition potential are under use as an oral hypoglycemic medicines to check hyperglycemia [60]. Furthermore,
218 exploration of α -glucosidase inhibitors is of supreme priority for finding novel anti-diabetic drugs [61].

219 3.7 Antiviral activity

220 The viral particles spread and replicates within the host cells, cause severe disturbances and conditions.
 221 Recently, many influenza viral epidemics has been out broke in many parts of the world. The annual report by
 222 World Health Organization (WHO) published early in 2018, explained that data from about all over the world
 223 laboratories has confirmed many incidents of epidemic influenza H1N1 2009 that caused almost 13,554
 224 mortalities [17]. The birds influenza virus mainly generated the oxidative stress and amplify the inflammations
 225 within the patient. Quercetin, 3,4-dihydroxybenzoic acid and methyl-3-hydroxybutanedioic esters, which
 226 were extracted from *C. speciosa* pose a synergistic effect during the treatment of avian influenza, hence proved
 227 as prospective and strong antiviral compounds [17]. Avian influenza is frequent and followed with virus
 228 invasion along with increased oxidative stress and heavy inflammations. Furthermore, numerous effects of the
 229 *C. speciosa* compounds have a potential and specialized role in curing avian influenza, particularly quercetin
 230 would be a strong anti-inflammation and anti-viral compound [17]. The Oleanolic acid extracted from *C.*
 231 *speciosa* (20µg/ml) robustly inhibits the replication of hepatitis B virus genome showed a powerful inhibition
 232 ratio (29.33%) [62]. These *C. speciosa* plant extracts contains powerful antioxidants in it that depict could
 233 potentially be used to cure new influenza A virus epidemics.

234 It is summarized that continuous research interests has explored plenty of natural compounds from *C.*
 235 *speciosa* plant. Such explorations of novel compounds from this plant has been said to possess strong medical
 236 importance. In certain disease arouse mainly of heavy oxidative stress are being replenished by the strong
 237 antioxidant nature of this plant. The flavonoids present in *C. speciosa* mainly reduces peroxide and LDL levels,
 238 remove DPPH and de-oxidize free cellular iron (Fe³⁺), and hence pose a strong antioxidant effect. Moreover, *C.*
 239 *speciosa* plant also contributed its immune modulatory and anti-inflammatory effects by reducing the
 240 expression of interleukins and related inflammatory factors. The various phytochemicals particularly the
 241 polysaccharides present in *C. speciosa* possess α -glucosidase inhibition potential and hence reduces
 242 hypoglycemic conditions. Similarly, anti-microbial and analgesic effects of the *C. speciosa* compounds are
 243 mainly following G-protein-AC-cAMP regulated signaling cascade to reduce the inflammation and
 244 deterioration of joints in arthritis rats. In different virus associated pathologies such as avian influenza,
 245 Quercetin, 3,4-dihydroxybenzoic acid and methyl-3-hydroxybutanedioic esters reduces the oxidative stress and
 246 expression of many inflammatory factors caused by the viral pathogen, and hence relive the pains and condition
 247 of the patient. Moreover, oleanolic acid present in *C. speciosa* efficiently inhibits the replication of hepatitis B
 248 virus genome.

249 4. Conclusions

250 It is concluded that *C. speciosa* have broad scope in industry and in medicines. Not only the leaves and
 251 fruits of *C. speciosa* plant, but various other parts which include roots, seeds, bark twigs, and flowers, all have
 252 long clinical trials history in curing many human ailments. However, the maximum accessible data concerning
 253 the chemical composition and their broad pharmacological properties of various parts of *C. speciosa* plants is
 254 quiet less that make it more appealing for indepth investigations.

255

256 **Conflicts of Interest:** The authors declare no conflict of interest.

257 **Author Contributions:** conceptualization, C.P.W. and W.F.H.; investigation, C.P.W.; writing—original draft
 258 preparation, W.F.H., J.H.W, M.F.N, H.S.L.; writing—review and editing, C.P.W.; supervision, C.P.W.; project
 259 administration, C.P.W.; funding acquisition, W.F.H.

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 262 Tingdong Yan (Duke-NUS Medical School, Singapore) in summary of pharmacological activities of *C.*
 263 *speciosa*.

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