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Mini Review

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

Weifeng Huang [1,†], Junwei He [2,†], Muhammad Farrukh Nisar [3], Hongshui Li [4] and Chunpeng Wan [5,*]

[1] Department of Microbiology and Immunology, Medical College, China Three Gorge University, Yichang, Hubei 443002, China; huangweifeng@ctgu.edu.cn
[2] Research Center of Natural Resources of Chinese Medicinal Materials and Ethnic Medicine, Jiangxi University of Traditional Chinese Medicine, Nanchang 330004, China; hjwjn2008@163.com
[3] Interdisciplinary Research Center in Biomedical Materials (IRCBM), COMSATS University Islamabad, Lahore Campus, Lahore 54000, Pakistan; farrukh.nisar@cuilahore.edu.pk;
[4] The Second People Hospital of Dezhou, Dezhou 253022, China; hbzy509@163.com
[5] Jiangxi Key Laboratory for Postharvest Technology and Nondestructive Testing of Fruits & Vegetables, Collaborative Innovation Center of Post-Harvest Key Technology and Quality Safety of Fruits and Vegetables, College of Agronomy, Jiangxi Agricultural University, Nanchang 330045, China;
* Correspondence: chunpengwan@jxau.edu.cn; Tel.: +86-791-83813185
† These authors contributed equally to this work.

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

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

1. Introduction

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

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

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

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

2. Chemical Constituents

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

2.1. Triterpenes

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

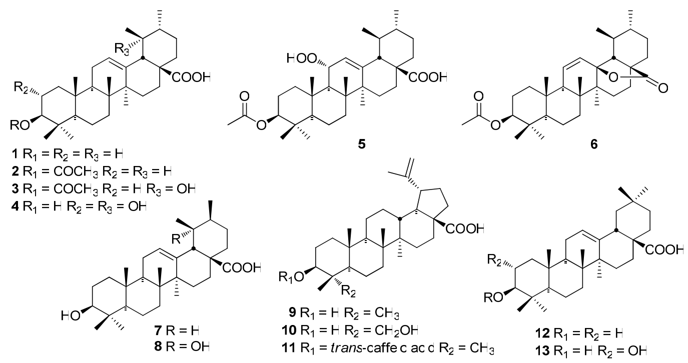

Figure 1. Chemical structures of triterpenes from *C. speciosa*.

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

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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

2.2. Sesquiterpenoids

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

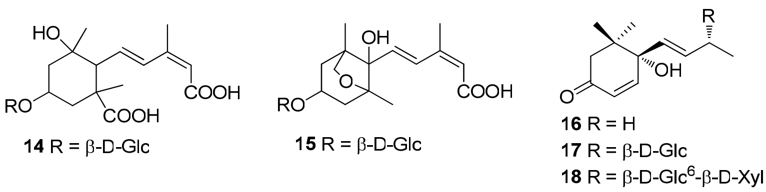

Figure 2. Chemical structures of sesquiterpenoids from *C. speciosa*.

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	(6*S*,7*E*,9*R*)-6,9-dihydroxy-4,7-megastigmadien-3-one 9-*O*-[*β*-D-xylopyranosyl(1→6)-glucopyranoside]	fruits	16,17,24

2.3 *Flavonoids*

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

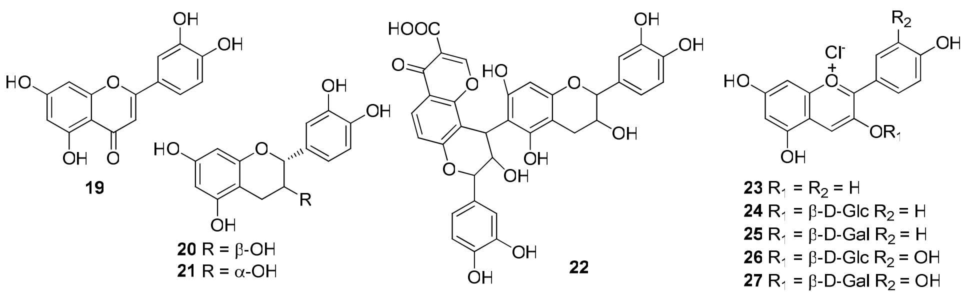

Figure 3. Chemical structures of flavonoids from *C. speciosa*.

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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	(-)-epicatichin	fruits	26
22	specpolyphenol A	fruits	27
23	pelargonidol chloride	petals	28
24	pelargonidin 3-*O*-β-D-glucopyranoside	petals	28
25	pelargonidin-3-galactoside	petals	28
26	cyanidin 3-β-*O*-glucoside	petals	28
27	cyanidin 3-*O*-β-galactopyranoside	petals	28

2.4 Phenylpropanoids

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

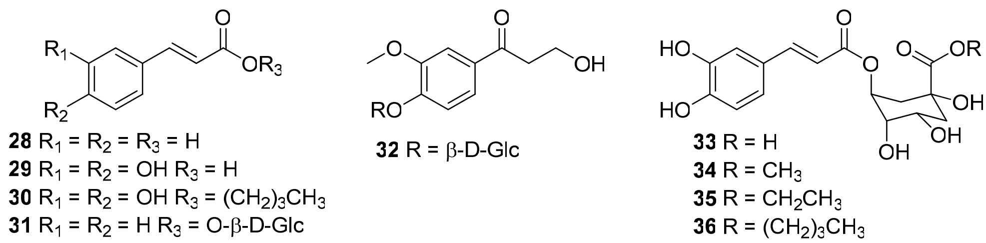

Figure 4. Chemical structures of phenylpropanoids from *C. speciosa*.

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-*O*-p-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-*O*-caffeoylquinic acid butyl ester	fruits	26

2.5 Phenols

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

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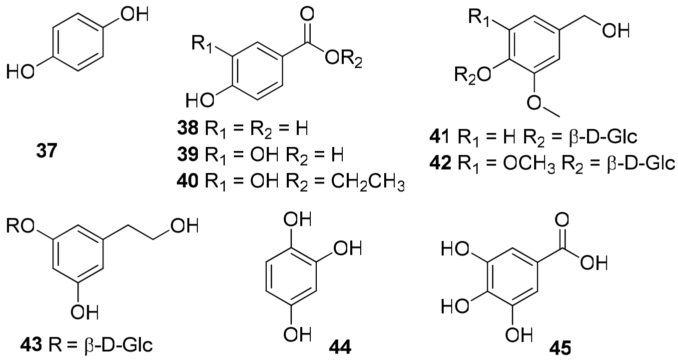

Figure 5. Chemical structures of phenolics from *C. speciosa*.

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-*O*-methylcrenatin	fruits	27
43	3,5-dihydroxyphenethyl alcohol 3-*O*-*β*-glucopyranoside	fruits	27
44	1,2,4-hydroxybenzene	fruits	24
45	gallic acid	fruits	20,24

2.6 Biphenyls

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

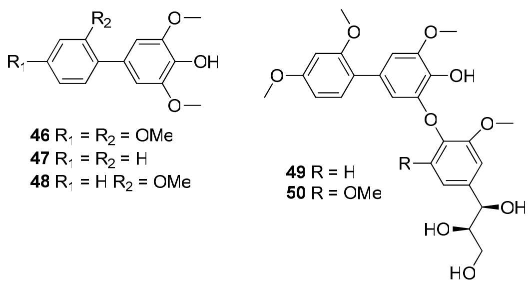

Figure 6. Chemical structures of biphenyls from *C. speciosa*.

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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

2.7 Others

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

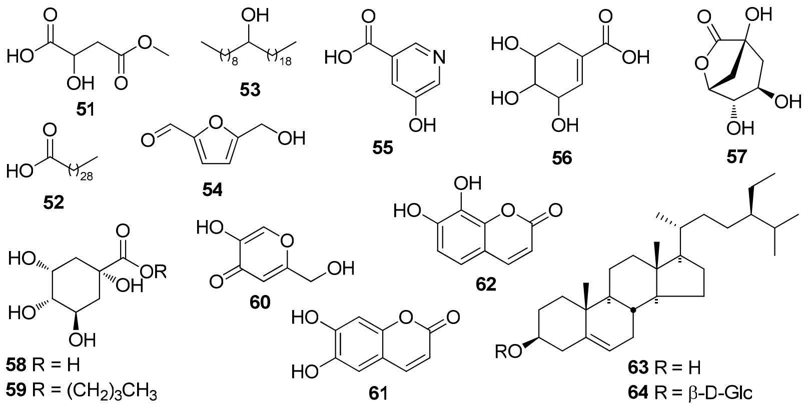

Figure 7. Chemical structures of other constituents from *C. speciosa*.

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

No.	Compounds	Parts	Ref.
51	3-methyl-3-hydroxylbutanedioic ester	fruits	17,25,29
52	triacontanoic acid	fruits	26
53	nonacosan-10-ol	fruits	15,18
54	5-hydroxyme thyl-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	daucosterol	fruits	15,18,22

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3. Pharmacological Activities

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

3.1 Anti-oxidant property

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

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

3.2 Anti-Inflammatory and analgesic activities

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

3.3 Anti-atherosclerotic effects

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

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

3.4 Anti-tumor and immunomodulatory activities

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

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

3.5 Anti-diarrhea

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

3.6 α-glucosidase inhibitory

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

3.7 Antiviral activity

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

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

4. Conclusions

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

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

Author Contributions: conceptualization, C.P.W. and W.F.H.; investigation, C.P.W.; writing—original draft 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 administration, C.P.W.; funding acquisition, W.F.H.

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