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A Short Commentary of the Dandelion and its Application for COVID-19

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Abstract: Dandelion is a herbal plant recorded in the China Pharmacopoeia of a People's Republic. It contains useful chemical constituents or active ingredients with pharmacological activities, such as anti-inflammatory, anti-viral, and antibacterial properties. Since COVID-19 has happened for over three years, there is no reasonable treatment up to the display. This brief commentary introduces the knowledge of dandelion, the background of COVID-19, and dandelion's mechanisms of pharmaceutical activities because it may be a conceivable candidate for combating SARS-CoV-2.

Keywords: dandelion; COVID-19; treatment; SARS-CoV-2.

1. Introduction

The Pharmacopoeia of a People's Republic in China recorded dandelion as a dry grass of *Taraxacum mongolicum* Hand. -Mazz., or Taraxacum borealisinense Kitam [1]. It has a shriveled and curly appearance. The root is conical, mostly curved, and 3 cm to 7 cm long. Its surface is tan and wrinkled. The root head has tan or yellow-white hairs, and some are fallen off. Leaves are basal, mostly shrunken, with dark gray-green color. The taste of dandelion is slightly bitter and cold in nature. Its functions are to clear heat and detoxification, dispel carbuncle and dissipate knots, dispel dampness, and dredge stranguria based on the traditional Chinese medicine (TCM) theory [2].

Dandelion contains flavonoids, terpenes, fenacs, dandelion pigments, phytosterols, sesquiterpene lactones, and coumarins. The major chemical constituents of dandelion include taraxasterol (TS), sesquiterpene lactones, caffecic acid, chlorogenic acid, *p*-coumaric acid, sinapic acid, ferulic acid, cichoric acid, taraxinic acid-β-D-glucopyranoside (Figure 1) [3].

Dandelion plants have been used for a long history of medicinal use and are presented around the world since some major chemical constituents, or active ingredients of dandelion with specific pharmacological activities, such as
(1) anti-inflammatory agent (e.g., taraxasterol) through metabolism [4];
(2) chlorogenic acid that scavenges free radicals which inhibit DNA damage and protect against the induction of carcinogenesis; activates the immune system to proliferate or increase the number of cytotoxic T-lymphocytes, macrophages, and natural killer cells [5];
(3) sinapic acid that suppresses SARS-CoV-2 replication by targeting its envelope protein [6];
(4) an apoptosis inhibitor and cardioprotective agent (e.g. ferulic acid) to combat cancer and heart diseases [7];

(5) chicoric acid in the treatment of HIV-1 and prolong the life span that lowers the risk of having age-related diseases [8].

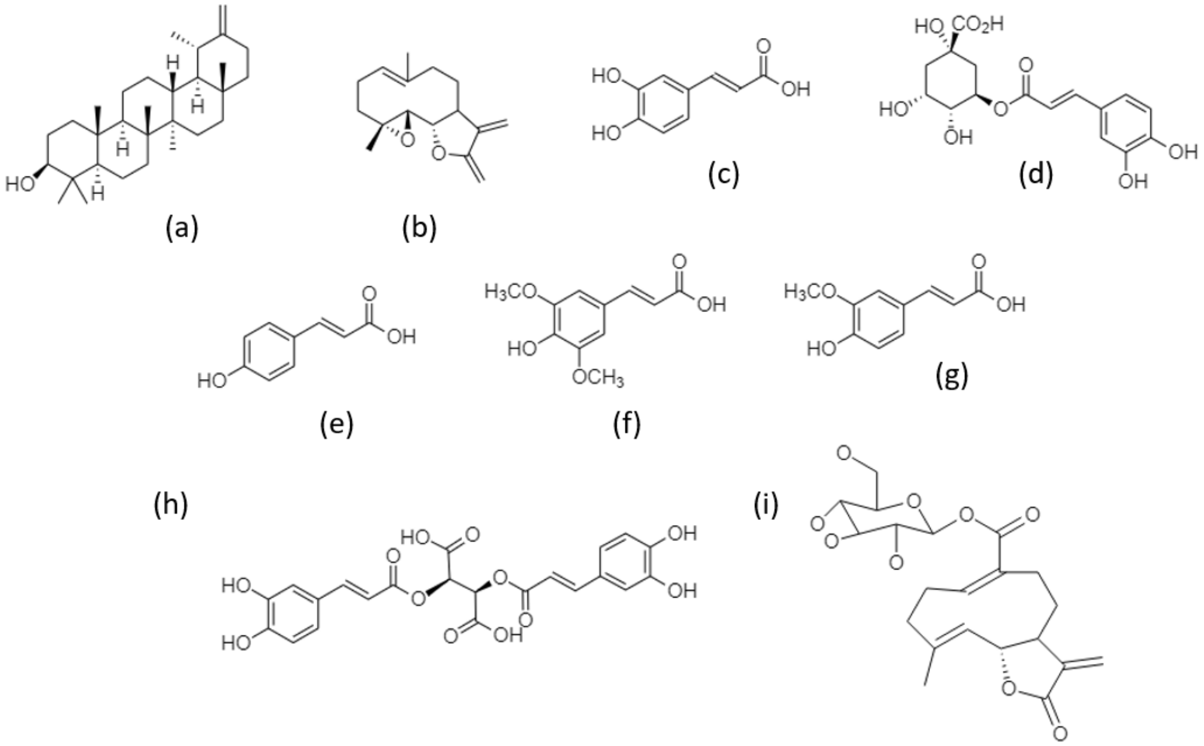

Figure 1. Chemical structures of **(a)** taraxasterol (TS), **(b)** sesquiterpene lactones, **(c)** caffecic acid, **(d)** chlorogenic acid, **(e)** *p*-coumaric acid, **(f)** sinapic acid, **(g)** ferulic acid, **(h)** cichoric acid, and **(i)** taraxinic acid-β-D-glucopyranoside.

In late December 2019, an episode of pneumonia with obscure etiology arose in Wuhan of Hubei province, named coronavirus disease (COVID-19) by the World Health Organization (WHO). It is an infectious disease caused by the SARS-CoV-2 virus [9].

The source of SARS-CoV-2 can be through droplets or direct contact with human-to-human. Preliminary analysis has shown that the SARS-CoV-2 genome (WH-Human 1) was closely related to the SARS-like coronavirus previously found in bats, with 96.2% similarly in the SARS-related coronaviruses (SARSr-CoV, and RaTG13). A novel bat-derived coronavirus, "RmYN02" shared 93.3% nucleotide identity with SARS-CoV-2 at the genome scale [10].

Most people infected with COVID-19 would develop mild to moderate illness and recover without special treatment. Fever, cough, diarrhea, a rash on the skin, difficulty breathing, or chest pain are common symptoms. It usually keeps the symptom for 5 to 6 days, even up to 14 days if this is serious [11].

2. Methods

China National Knowledge Infrastructure (CNKI), WanFang Data, PubMed, Science Direct, Scopus, Web of Science, Springer Link, SciFinder, and Google Scholar were the electronic databases used to search some keywords, such as "Dandelion", "Dandelion + SARS-CoV-2", "COVID-19", “Dandelion + COVID-19”, etc., and at least 20-30 journal were reviewed. All eligible studies are analyzed and summarized in this commentary.

3. Research Process

COVID-19 has been attacking the world for over three years, and there is still no possible prevention and treatment for the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). However, traditional Chinese medicine (TCM) is a possible candidate for combating SARS-CoV-2, such as dandelion, because of its anti-inflammatory, anti-viral, and antibacterial properties (Table 1).

Table 1. Previous studies of pharmacological activities for dandelion.

	Zhang *et al*. (2012) [12]	**Jiao *et al*. (2022) [13]**	**Zígolo *et al*. (2021) [14]**	**Jeon *et al*. (2008) [15]**	**Rodino *et al*. (2015) [16]**
Objective	To investigate the *in vitro* anti-inflammatory activity of taraxasterol in lipopolysaccharide (LPS)-induced RAW 264.7 murine macrophages	To evaluate the current state of research and provide an overview of the possible applications of taraxasterol in various diseases	To evaluate compounds of natural origin, mainly from medicinal plants, as potential SARS-CoV-2 inhibitors through docking studies	To demonstrate that the ethanol extract of Taraxacum officinale possesses anti-angiogenic, anti-inflammatory, and anti-nociceptive activities	To study the antibacterial and antioxidant activities of ethyl acetate extract of Urtica dioica and Taraxacum officinale
Function	Anti-inflammatory	Anti-viral	Anti-viral	Anti-inflammatory	Antibacterial
Result	Taraxasterol inhibited NO, PGE2, TNF-α, IL-1β, and IL-6 production in LPS-induced RAW 264.7 macrophages in a dose-dependent manner	Taraxasterol reduced the secretion of HBsAg, HBeAg, HBV DNA, and intracellular HBsAg l, which decreased the protein expression levels, such as binding protein 1 (PTBP1) and sirtuin 1 (SIRT1) in HepG2.2.15 cells	Molecular docking was performed using AutoDock, which selected the plant actives with the highest affinity towards the virus, such as taraxasterol with -8.11 the best energy binding value for SARS-CoV-2	Taraxacum officinale ethanol extract (TEE) showed a scavenging activity in the 1,1-diphenyl-2-picrylhydrazyl (DPPH) assay, a diminishing effect on intracellular reactive oxygen species (ROS) level, and an anti-angiogenic activity in the chicken chorioallantoic (CAM) assay, as well as inhibited the production of exudate and significantly diminished nitric oxide (NO) and leukocyte levels in the exudate	Ethyl acetate extract of nettle was more effective on Aeromonas hydrophila, Salmonella typhi, *Staphylococcus aureus*, *Bacillus cereus*, Escherichia coli, and bacterial isolates than dandelion
Significance	Taraxasterol with an anti-inflammatory effect by blocking the NF-κB pathway	Taraxasterol with an anti-viral effect by decreasing the protein expression levels of the host factors	Hydrogen bonds and hydrophobic interactions between taraxasterol flight against COVID-19 that could potentially be evaluated	Taraxacum officinale contains anti-inflammatory activities through its inhibition of NO production and COX-2 expression and/or its antioxidative activity	The ethyl acetate extract of dandelion can inhibit the growth of both Gram-positive bacteria (*Staphylococcus aureus*, *Bacillus cereus*) and Gram-negative bacteria
Disease	Pneumonia	Hepatitis B	SARS-CoV-2	Pulmonary Edema	Bacterial coinfection

On the 31st of March, 2022. the World Health Organization (WHO) recently released the "WHO Expert Evaluation Meeting on Chinese Medicine Treatment of COVID-19" under the relevant section of its official website, which understood and affirmed their safety and effectiveness [17]. However, dandelion possesses anti-inflammatory, anti-viral, and antibacterial properties; its function and effectiveness against COVID-19 are still to be investigated (Table 2).

Table 2. Current studies of Dandelion against COVID-19.

	Tran *et al*. (2022) [18]	**Jiao *et al*. (2022) [19]**	**Jalili *et al*. (2020) [20]**
Objective	Common dandelion (Taraxacum officinale) efficiently blocks the interaction between ACE2 cell surface receptor and SARS-CoV-2 spike protein D614, mutants D614G, N501Y, K417N, and E484K in vitro	Dandelion, a Pest, or a Remedy? A Trends Analysis through Big Data	An overview of therapeutic potentials of Taraxacum officinale (dandelion): a traditionally valuable herb with a rich historical background
Function	Anti-inflammatory	Anti-inflammatory and Antibacterial	Anti-inflammatory and Lung-protective
Result	Dandelion blocked the protein-protein interaction of spike S1 to the human ACE2 cell surface receptor, and an infection of the lung cells using SARS-CoV-2 spike pseudotyped lentivirus particles was efficiently prevented by its extract and the virus-triggered pro-inflammatory interleukin 6 secretion	Dandelion was a natural diuretic, which caused more urination, and removed excess sugar from the body since excess sugar led to kidney disease and diabetes that is more potent to be infected by SARS-CoV-2	The pharmacological and therapeutic features of dandelion in traditional medicine positively influence dyslipidemia, hematological profile, stomach motility, fatigue, and bifidobacteria
Significance	Dandelion effectively inhibition of protein-protein interaction between the human virus cell entry receptor ACE2 and SARS-CoV-2 spike, as well as overexpressing the ACE2 and ACE2/TMPRSS2 protein for preventing lung infection	Dandelion increases the immunity system with less significant side effects than drugs to the human body	Dandelion lacks toxicity and side effects, which is considered complementary medicine, but the efficacy of dandelion in clinical use would be required for further investigations
Target	SARS-CoV-2	SARS-CoV-2	SARS-CoV-2

4. Discussion

COVID-19 is caused by a virus, “SARS-CoV-2”, which attaches to angiotensin-converting enzyme 2 (ACE2) in the respiratory tract for replication and is infected with the other molecules. An immune system would respond to the infected cells, causing inflammation and leading to the damage of air sacs, scarring, hardening, and even filling with fluid, resulting in edema of the lung.

4.1. Anti-inflammatory.

SARS-CoV-2 makes the immune system overactivation and produces a cytokine storm that constitutes lung injury and multiple organ failure [21]. The viral infection and dysregulation in the immune system contribute to disease pathogenesis [22]. A sub-unit E protein of SARS-CoV-2 that promotes the nuclear factor kappa B (NF-κB) signaling pathway producing and releasing inflammatory cytokines, such as tumor necrosis factor (TNF) and interferon (IFN) [23].

The TNF and interferon-gamma (IFN-γ) attach to respiratory tract receptors, which activate the inflammatory, leading to cell death, “PANoptosis”. This is an inflammatory cell death pathway. It first cleaves inactive full-length gasdermin into its active form. The pyroptosis occurs through the formation of membrane pores, apoptosis within extrinsic pathways, and finally necrosis via the activation of mixed lineage kinase domain-like (MLKL) in an immune system. The JAK/STAT1/IRF1 axis is activated by the co-processing of TNF-α and IFN-γ, resulting in nitric oxide (NO) production and APoptosis mediated by caspase-8/FADD for inflammation and damage to tissues [24]. TNF-α production is critical for the synergistic induction of NO synthesis in LPS-stimulated macrophages. IL-1β and IL-6 are the key pro-inflammatory cytokines and endogenous mediators of LPS-induced fever, leading to cellular or tissue damage during inflammation [25-27]. Taraxasterol acts as an anti-inflammatory agent that inhibits TNF-α, IL-1β, and IL-6 production in a dose-dependent manner in LPS-stimulated RAW 264.7 cells [1].

Cichoric acid undoubtedly alleviates LPS-induced lung damage and reduces inflammatory cell immersion as well as alveolar hemorrhage. Lung wet/dry weight ratio and protein concentration are 2 crucial indicators of lung injury. The LPS automatically increases the wet/dry weight ratio and protein concentration in bronchoalveolar lavage fluid (BALF), and cichoric acid as LPS for triggering inflammatory cell infiltration, leading to high expression of cytokines in the exudative phase of LPS-induced acute lung injury [28-29]. Cichoric acid also unquestionably decreases the number of neutrophils and macrophages, which are associated with the suppression of cytokine production, including TNF-α, IL-1β, and IL-6. This result protects cichoric acid against LPS-induced acute lung injury for its anti-inflammatory effect [30].

4.2. Anti-viral and antibacterial.

Previous epidemic and pandemic outbreaks of viral respiratory infections have reported bacterial infections complicating initial viral illness. Bacterial coinfection was reported in up to 30% of critically ill patients and 12% of hospitalized patients not requiring ICU admission during the 2009 A(H1N1) influenza pandemic [31]. There are scant data on bacterial coinfections from patients infected with SARS-CoV-1 and MERS-Co-V [32]. The current knowledge of pathophysiology for SARS-CoV-2 is evolving, and the pathogenesis of bacterial coinfection is still incomplete. This is postulated that viral damage of epithelial cells in the lower airway, coupled with mucociliary dysfunction, facilitates binding to cell surfaces of pathogenic bacteria aspirated from the nasopharynx [33]. Bacterial coinfections increased the severity of respiratory viral infections and were frequent causes of mortality in influenza pandemics but have not been well characterized in patients with COVID-19. However, the ethyl acetate extract of dandelion has been shown to inhibit the growth of Gram-positive bacteria (*Staphylococcus aureus*, *Bacillus cereus*) and Gram-negative bacteria [16]. Dandelion is an anti-viral and antibacterial agent for the prevention of COVID-19.

5. Conclusion

Dandelion is a possible candidate for combating SARS-CoV-2 because it possesses anti-inflammatory, anti-viral, and antibacterial properties. However, much more work needs to be done, including some safety assessments, e.g., dosage and herb-drug interaction of clinical studies on the human body require further investigation.

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Conflicts of Interest

The authors declare no conflict of interest.

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