

Mechanism of Herbal Medicine and Food Dandelion Effects May be Related to RNA or DNA Regulation: A Review

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Abstract

Background: A dandelion is a common plant with a global growth distribution that has been used as a medicinal and food with no adverse effects. **Purpose:** In this article, the products and effects of dandelions are reviewed to help further in-depth studies and develop more products derived from dandelions in the future. **Method:** The literature about dandelion in various databases such as Pubmed is searched. **Results:** Dandelions have many effects, such as virus inhibition, anti-tumor activity, nutritional value, anti-aging, potential as a vaccine and alleviation of heat stress. The mechanism underlying these effects is analyzed and it was found that dandelions were regulated by RNA or DNA. **Conclusion:** As a medicinal and food, dandelions are safe and have many effects. Many products derived from dandelions have been developed. The metabolic regulation is related with ribonucleic acid or possibly deoxynucleic acid. Further in-depth studies should be conducted on the regulation of dandelions through RNA or DNA. There will likely be more products derived from dandelions in the future.

Keywords

Dandelion, Herb, Medicine, Food, Nutrition, RNA, DNA, Metabolism

1. Background

The plants used in medicines and foods are very important for people.

Sir Frederick Keeble published a lecture in *Nature* 1 (25 December 1937) entitled “The Basis of Life on Earth: Soil and Greenery”, in which he hypothesized that the health and strength of people and their evolution, and the permanence

of human societies depend on the soil and the green plant. The term “green herb” in Hebrew has the broadest meaning and includes all herbs of edible value to both man and beast [1].

Based on the World Health Organization, 80% of the world’s population relies on indigenous medicinal plant remedies. Herbs use fruits and vegetables as drying materials or their extracts to treat various diseases and maintain health. Licorice has been used in China and Europe since prehistoric times. Licorice root is one of the most widely used herbal preparation to treat liver diseases [2].

Over the course of thousands of years, ancient Rome, ancient India, Arab, ancient Egypt, ancient Babylon and Traditional Chinese Medicines have emerged. Although these medical systems have their own differences, the medical systems all focus on herbal and spiritual remedies. Ancient traditional medicine is different from modern Western medical thoughts. Specifically, ancient traditional medicine tends to regulate the characteristics of the human body rather than focus on viruses and diseases, which adjust the person to a state of balance with nature through herbal meditation and sports lifestyle. Ancient Greek physicians believe that good health comes from a balance of natural forces. A compilation of many plants and drugs derived from plants, highlight diuretics, laxatives, and emetic drugs. Ayurvedic medicine of ancient Indian traditional medicine is still popular today. Ayurveda has aroused the interest of researchers from Europe, the US, and other countries worldwide, who have joined in the study of Ayurveda. Ayurveda has a growing role in Europe [3]. Like Traditional Chinese Medicine, most Ayurvedic healing requires mixed herbs.

Due to extreme climate conditions, such as the melting of Antarctic glaciers, virus exposure in frozen soil poses a threat to human beings, and high temperatures cause oxidative stress in the body, which leads to a greater need for plant food or phytomedicine. Because the population is large, sequelae of coronavirus disease 2019 (COVID-19), tumors, chronic diseases, and psycho-emotional disorders, there is a greater need for plant food or phytomedicine. Traditional medicine involves a holistic strategy for the human body to integrate treatment with culture, environment, and psychology. The new future medicine must merge ancient healing with the innovations of modern medical science and technology to increase longevity and improve the quality of life worldwide [4].

Based on the importance of herbs and the need for global health, we have summarized the effects of dandelions and the mechanism underlying these effects. This review may help further in-depth studies on dandelions from RNA or DNA regulatory mechanisms and help develop more products derived from dandelions in the future.

The various effects of dandelions reviewed in this article include the virus inhibition, anti-tumor activity, nutritional value, anti-aging, potential as a vaccine and alleviation of heat stress, which is comprehensive and seems scattered. However, these effects are intrinsically related. The virus and aging can help form tumors. The nutrition is related with virus, tumor and aging. The mecha-

nims of these effects are related with inflammation, oxidation and endoplasmic reticulum stress. The mechanisms are related or potentially related with lncRNA, mRNA, miRNAs, RNA chemical modification, RNA polymerases and rDNA methylation.

2. Components, Related Studies, and Dandelion Products

Dandelions are common plants and the global growth distribution is enormous. Dandelions have been widely used as folk medicine and food, and no adverse effects have been reported in the treatment of liver and kidney diseases, cancer, and some diseases affecting women, such as breast and uterine cancers. Dandelions contain many nutrients beneficial for health, especially for women. We found that dandelions inhibit the hepatitis B virus by regulating the expression of host proteins and inhibiting inflammatory mediators IL-6 [5]. In addition, according to the practical experience of people, dandelions are also resistant to bacteria. Its soak water lowers the body temperature, is conducive to gastrointestinal peristalsis, nourishes the digestive system, and other functions.

There are six biosynthetic pathways [6]: polyphenols; phenylpropanoids; methylerythritol 4-phosphate (MEP) and mevalonate (MVA); natural rubber; sesquiterpenoid and triterpenoids; and inulin. There are 3 interconnections among the biosynthetic pathways in *Taraxacum* species (dandelions), which are as followed: sesquiterpenoid and triterpenoids, sucrose, and phenolic acid. The potential of dandelions as sources for medicines and foods, as well as raw materials for industrial production, has led to intense, multi-focused research involving these plants.

Owing to the medicinal properties and a source of natural rubber, the biosynthesis and the pharmacologic activities of bioactive metabolites, such as phenolic acids, flavonoids, and triterpenoids in dandelions are being investigated and studied in depth, while studies on transcriptional regulation are at an initial stage [6].

Liu *et al.* [6] have proposed future studies: 1) Although the number of *Taraxacum* spp. germplasm resources are large, these species need to be further evaluated and a complete comparison and summary study of the resources must be conducted. 2) The largely unknown downstream pathways are in need of study, although many upstream biosynthetic pathways involved in various bioactive compounds have been studied. 3) The underlying mechanisms, such as transcription factors (TFs) and signaling pathways, regulating polyphenol and terpene biosynthesis, have rarely been studied in dandelions. Future studies should establish the metabolic regulatory network of different compounds, integrating plant signaling pathways and environmental regulators, such as light, drought, and salt stress. The molecular mechanisms underlying the correlations between the environment and secondary metabolites in dandelions should be the focus of research.

The relationship between environment, genotype, and secondary metabolites

needs to be elucidated, which provides a targeted selection of dandelion varieties and further product development [6]. **Figure 1** shows various products sourced from *Taraxacum* spp., including food, medicine, and rubber materials. There should be more dandelion-related products in the future.

3. The Mechanism Underlying Virus Inhibition for Dandelions Related to RNA

Dandelions or dandelion components have a role in virus inhibition, such as HIV-1, influenza virus, and Epstein-Barr virus [5]. HBsAg, HBeAg secretions, and HBV DNA are inhibited by dandelion (*Taraxacum* spp.) extracts, but the difference in values is not large. Taraxasterol is one component of dandelion extracts. The mechanism underlying HBV inhibition involves inhibiting the expression of PTBP1 and SIRT1 proteins in the host. Dandelions and taraxasterol extracts both significantly decrease the IL-6 level of HepG2.2.15 and THP-1 co-culture supernatants, hence it may be that the more important role of dandelions is to regulate the body's immune balance.

It is known that greater than 80% of Chinese patients with coronavirus disease 2019 (COVID-19) were treated with traditional Chinese medicine (TCM). Herbal small RNAs (sRNAs) in ToujieQuwen (TQ) granules are novel functional

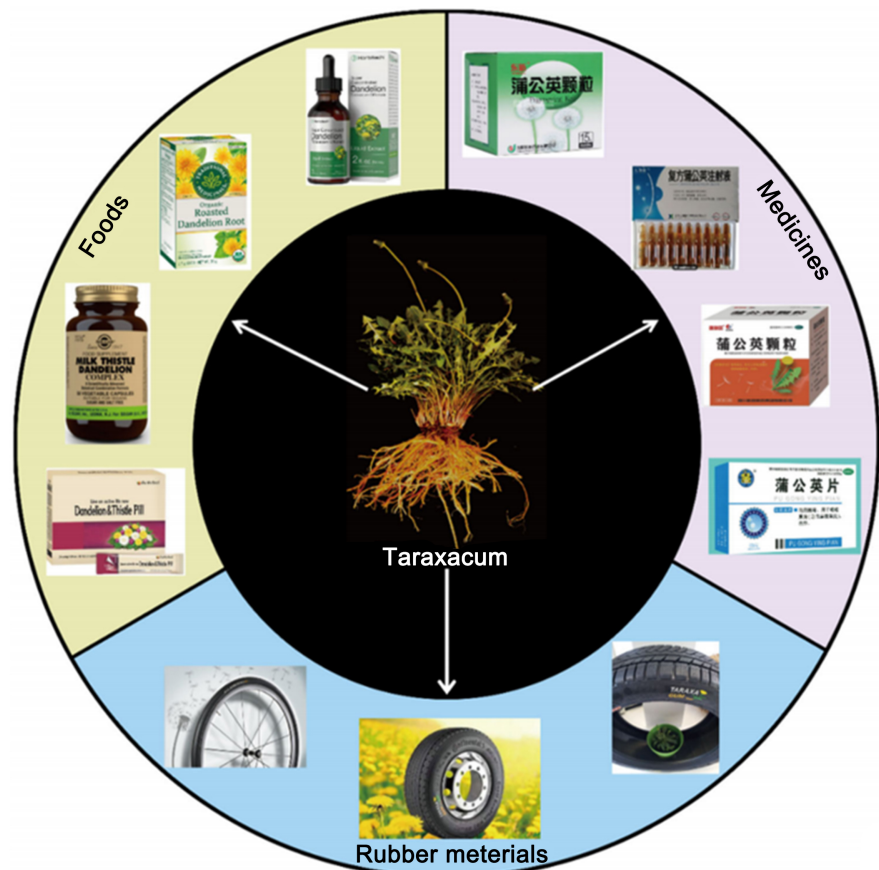


Figure 1. Variety of products sourced from *Taraxacum* species.

components that can effectively alleviate genetic disorders in COVID-19 patients [7]. Thousands of double- and novel-increased sRNAs have been identified in peripheral blood mononuclear cell samples collected from patients with mild COVID-19 before and after the consumption of TQ granules. The results of pathway enrichment analysis show that the predicted targets of sRNA are clustered into inflammatory and antiviral immune responses. Hence, the antiviral mechanism underlying dandelions has been studied not only from host proteins (PTBP1 and SIRT1) or host immune responses, but also from genes in the future.

4. Inhibitory Effect of Dandelions on Cancers Related to RNA or DNA

Multicomponent herbal medicines have the potential to treat a variety of multifactorial disorders. Although both endothelial cells and tumors are inhibited by targeted agents currently in clinical use, there are 10 targets in tumor and endothelial cells. The combinations of targeted agents are often two targets for cancers [8]. Hence, herbal medicines with multiple components have the advantages of multi-targets and safely balance the body.

4.1. Inhibition of Proliferation and Migration of Gastric Cancer (GC) for Dandelions by Regulating Long Non-Coding (lnc) RNA

GC is one of the most common tumors worldwide. Metastatic gastric cancer is difficult to treat with immunotherapy, radiation, and chemotherapy. Zhu *et al.* have reported that dandelion root extract can selectively and effectively inhibit the proliferation and migration of human stomach cells [9]. It is known that lncRNA promotes the occurrence of many tumors. The expression of transcript 1 associated with lncRNA colon cancer (CCAT1) is downregulated after dandelion treatment of GC cells, and CCAT1 downregulation inhibits GC proliferation and migration.

4.2. Inhibition of Hepatocellular Carcinoma (HCC) and Cancer-Related Diseases by Dandelions

Dandelion polysaccharides reduce the iron load to reduce the risk of HCC cells and transplanted tumors [10]. Dandelions also inhibit HCC proliferation by inhibiting PI3K/AKT/mTOR and inducing cell cycle arrest [11]. Dandelion leaf extract is a promising kidney protector for cisplatin-induced nephrotoxicity through antioxidant, anti-inflammatory, and anti-apoptotic activities [12]. In addition to the above several inhibition mechanisms of HCC or cancer-related diseases, similar to the inhibitory mechanism underlying GC, dandelions may inhibit HCC and other diseases by inhibiting lncRNA. In the future, we may study lncRNA inhibition of dandelions for other cancers.

4.3. Dandelions for the Treatment of Cancers Affecting Women, Such as Breast or Cervical Cancer

The common name of *Taraxacum mongolicum* is dandelion, which is a herb

medicine with anti-cancer activity that has been utilized to treat hyperplasia of mammary glands and mammary abscesses from ancient China to date [13].

Breast cancer stem cells have a role in breast cancer, including initiation, metastasis, recurrence, and drug resistance. The proliferation of breast cancer stem cells is efficiently inhibited by the extracts of *Taraxacum officinale* [14].

As one component of dandelions, the effect of luteolin on human breast cancer is detected using gene expression array inferring novel genes. The mRNA expression profiles are analyzed by a bioinformatics approach of gene expression array analysis [15].

Dandelion extract inhibits the proliferation of triple-negative breast cancer cells by interfering with unsaturated fatty acid metabolism and glycerophospholipids. The mechanisms against this cancer by dandelions are uncovered by a combined molecular pharmacology, metabolomics, and network pharmacology approach [16]. This study indicates that the multi-target mechanisms by dandelions against this cancer use a combined, comprehensive approach. These findings will provide evidence for further research and may lead to the development of highly effective treatments based on dandelions for triple-negative breast cancer [17]. Dandelion extract induces apoptosis, which is related to endoplasmic reticulum stress in triple-negative breast cancer cells and cervical cancer cells [13] [18].

The mechanism underlying gynecologic cancer inhibition by dandelions has been studied extensively from network pharmacology, metabolomics, endoplasmic reticulum stress, and breast cancer stem cells. In the future, we may study the mechanism by which dandelions regulate RNA or DNA in gynecologic cancers.

4.4. Dandelions for the Treatment of Cancer-Promoting Factors, Such as Alcohol or Depression

In a recent study [19], volunteers consume alcohol, then are given dandelion juice daily for 7 days. Dandelion juice supplementation alleviates oxidative stress and hangover syndrome through elevated plasma acetaldehyde dehydrogenase and antioxidant enzyme systems in healthy males. Moreover, erythrocyte glutathione reductase, catalase activity, and protein expression of the dandelion supplementation group are significantly increased.

Multiple medicinal plants used during the Arab Islamic period (7th-14th centuries AD) treated malignancies of the urinary tract. Using ancient Greek medicine, Arab scholars quickly understand the nature of this deadly disease and described new types of cancer to distinguish urinary tract malignancies from other diseases, such as infections, and suggest new treatments, including surgery and non-invasive treatments. The herbs that followed Diosculid and Galen flourished in the Arab world. Malignant tumors of the urinary tract are identified and herbs are used to slow tumor progression. Herbs are introduced to reduce cancer symptoms and Arabic herbs may still benefit against cancer, primarily for

palliative care [20].

In addition, the prevalence of depression is substantial. Depressed patients are imbalanced and prone to cancer. Li *et al.* [21] have reported that depression-associated tumor locations are consistent with tumor suppression networks (89%) by manually tracking brain lesion location to a standardized brain template based on the ITK-SNAP descriptive literature. The expression of inflammatory mediators is generally higher in patients with depression, and the most herbs generally have anti-inflammatory effects. People need more traditional medicine plant therapy and other therapies to balance and restore the human body environment, and to reduce the probability of cancer.

5. Nutritional Value of Dandelions Can Be Studied through RNA Regulation

Dandelion leaf extracts have an effective protective effect against hepatotoxicity and genotoxicity induced by sodium dichromate. Histopathologic observations show that sodium dichromate causes acute liver injury, hepatocyte necrosis, and DNA breakage. The liver is an important nutritive metabolic organ. Dandelions have a protective effect that maintains normal nutritive metabolism by protecting the liver [22].

DNA microarray analysis showed that dandelion extract has an important role in lipogenesis and lipid metabolism by regulating the expression of many genes and lncRNA, and can be used as a potential candidate for the treatment of obesity [23].

Curcumin, an herbal component from medicinal and edible ginger, has regulatory effects on non-coding RNA. Ginger (*Zingiber officinale*) belongs to the genus *Zingiber*, which is known as a perennial herbaceous plant. In East and Southeast Asia, ginger is among one of the most important medicinal and edible crops. Xing *et al.* [24] conducted a study involving targets and related miRNAs involved in ginger development. Further experiments are required to characterize the role of miRNAs in the regulation of ginger development. It is well-known that functional genome expression profiles help demonstrate the mechanism of action for curcumin. A variety of platforms, reflecting the progress of functional genome technology, can be used to study these actions both *in vitro* and *in vivo* [25].

Dioscin, a herbal component of *Dioscorea zingiberensis*, regulates non-coding RNA. The miRNAs in Ishikawa cells (human endometrial cancer cells) have changed greatly after dioscin treatment, and the significantly up- and down-regulated miRNAs have been initially screened [26]. This study indicated that dioscin participates in regulating the migration and invasion of endometrial carcinoma (EC) cells according to high-throughput sequencing data of RNA expression (miRNA and mRNA). It is more important than the miRNA-target gene network screens out related hub genes and miRNAs; however, further studies are required to fully demonstrate the exact complex regulatory mechanism

related to miRNAs and their target genes that participate in the inhibitory effect of dioscin on EC cell metastasis. My opinion is that the herb treatment should focus more on the body balance role, not the anti-cancer role.

Abnormal miRNA expression occurs in psoriasis, and some dietary compounds have potential effects on endogenous miRNA synthesis. It is known that natural agents, such as polyphenolic derivatives present in fruits and wine, presumably exert anti-inflammatory and antioxidative properties. These natural agents have the ability to modulate miRNA expression in various chronic diseases. A report has recently demonstrated that during animal food absorption, a significant amount of miRNAs may be absorbed; however, the absorption of plant-derived miRNAs is not obvious [27]. In the future, the interaction between the animal and plant foods on human health and well-being should be studied. These interaction data sets can be interpreted from the theory of TCM [28].

Metabolism is closely related to nutrition, while nutritious plants change human metabolism. Barnett have reported that metabolomics data sets can be used to identify the overall pattern of individual metabolites [28]. The purpose of metabolomics is to answer some important questions about metabolite level changes: Is a metabolite correlated with the degree of inflammation? Does a metabolite predict the onset or remission of inflammation? What constitutes effective monitoring for health status or the impact of a nutrient intervention?

6. Mechanism of Anti-Aging for Dandelions May Be Related to RNA

Aging is associated with a wide range of physiologic changes, including degeneration of neuronal systems, hair loss, skin wrinkling, and skeletal muscle weakness. Studies have previously identified numerous molecular biomarkers involved in such changes, but the regulatory mechanisms, functional effects, and regulatory strategies remain to be thoroughly investigated [29].

A daily intake of 400 mg of dandelion extract complex improves the quality of life in elderly male respondents and has the potential to reduce or alleviate menopausal symptoms [30]. Dandelion extract has a protective effect against drug-induced liver injury induced by acetaminophen in rats, and aging begins in the liver, which may be additional evidence for a delay in aging [31]. Dandelion extracts protect human skin fibroblasts from ultraviolet b damage and cellular senescence [32].

Aging is related to RNA regulation, and the anti-aging mechanism underlying dandelions can be further studied from the regulation of RNA.

Lee *et al.* [29] performed next-generation DNA methylation and RNA sequencing on blood samples from 51 healthy adults 20 - 74 years of age, identifying epigenetic and transcriptome biomarkers associated with aging to help develop therapeutic strategies for anti-aging.

Epigenomics analysis highlights the role of RNA chemical modification in various biological processes. Specifically, N6-methyladenosine (m6A) is the most

abundant internal modification of eukaryotic mRNA and is functionally related to multiple aspects of RNA metabolism, with m6A playing a role in processes, such as learning and memory. In fact, m6A is positively correlated with transcriptional expression, and m6A co-regulates transcriptional changes in gene expression of the hippocampus in elderly mice [33].

Ma *et al.* [34] analyzed the data of 1865 brain samples that covered 9 brain regions in 1074 unrelated subjects to identify interregional differences in RNA editing within the transcriptome. Whole proteomic verification results showed that RNA editing events affect protein expression in the brain tissues of elderly patients and patients with Alzheimer's disease, and only a small part of editing events occur at the protein expression level, indicating the importance of RNA regulation.

Genome-wide RNA polymerase stagnation affects the transcriptome during aging, and accumulation of DNA damage deteriorates basal transcription, thereby establishing age-related transcriptome and leading to dysfunction of key aging signature pathways, such as nutrient sensing, autophagy, and immune function. This transcriptional stress is caused by endogenous DNA damage, and age-related transcriptional stress is evolutionarily conserved from nematodes-to-humans [35].

Ribosome biogenesis requires the synergistic action of all three nuclear RNA polymerases (Pol I-III) in eukaryotes. Pol I transcription of these rRNA genes (rDNA) is a key regulatory step in ribosome production. RNA polymerase I transcription is involved in regulating development, disease, and aging. RNA polymerase I, rDNA integrity, and activity may be involved in aging [36].

Gene expression is the combination of many processes, including transcription, pre-mRNA processes, nucleoplasmic transport of mRNA, translation, mRNA degradation, and protein modification and degradation. Many changes in gene expression programs occur during development, differentiation, and aging. These changes are reflected in mRNA and protein levels. In fact, mRNA degradation is now emerging as an important locus of control and a major contributor to gene expression. Moreover, mRNA degradation processes in eukaryotes and some of the molecular mechanisms that alter the rate of degradation of specific mRNA lead to major genetic changes during development and aging [37].

In a 9-year follow-up study, methylation levels at one of the CpG sites analyzed are negatively correlated with both cognitive ability and survival chance. The methylation profile of rDNA may represent a potential biomarker of aging, with lower rRNA expression in highly-methylated samples. It has been confirmed that epigenetic modification of rDNA changes with age [38].

7. Potential Applications of Dandelions in RNA Vaccines

In the past few decades, with the rapid development of biotechnology, vaccines have been developed at a fast pace. A variety of human/veterinary vaccines include hepatitis B, BCG, influenza, and foot-and-mouth disease vaccines. The

new types of vaccines include genetic vaccines, such as RNA, synthetic peptide, and purified subunit vaccines; however, it has been shown that the immunogenicity of these new vaccines is relatively weak. Vaccine adjuvants assist enhancement of the immune response to antigens. Chinese herbal polysaccharides, a promising choice for a vaccine adjuvant, have the advantages of immune regulation, good biocompatibility, biodegradability, low toxicity, and safety. The results of various studies have shown that polysaccharides isolated from TCM have a powerful immune-enhancing effect. Some problems associated with polysaccharides are the purity and structure of polysaccharides [39]. Hence, in my opinion, water extracts from TCM are used in combination with RNA vaccines in the form of oral preparations or other forms, which may be better than the isolated polysaccharides or other components. This treatment strategy is particularly important in the context of emerging and frequent outbreaks of infectious diseases.

8. Heat Regulation of Dandelions May Be Related to RNA

Dandelions are common food plants. Dandelions can be soaked in water to relieve heat stress, which is especially conducive to health under extremely hot weather. Dandelions also have a role in resisting bacteria, thus are beneficial to gastrointestinal peristalsis and nourishing the digestive system. Dandelions contain a variety of healthy and nutritious active ingredients, that are especially good for women's health.

High temperature not only causes a harmful impact from heat stress, but also leads to severe economic loss in poultry production. Some thermoregulatory herbs or herb components reduce deleterious effects, such as immunosuppressive effects and the production of oxidative stress caused by heat stress. Oxidative stress induces injury of the cells. The immunosuppressive effects make the body susceptible to infection [40]. Some thermoregulatory herbs contain ginger, or herb components, such as resveratrol. Ginger increases total antioxidant potential, increases digestibility, and improves metabolism. The mechanism underlying thermoregulatory dandelions can be studied from metabolic regulation and regulatory RNA.

Capsicum has the ability to induce gustatory sweating to lower body temperature for people living in hot climates. The recipes from 36 countries contain spices and there are more pungent spices in hotter countries. A number of medical papyri that existed thousands of years ago demonstrated the use of herbs in the treatment of various human diseases in ancient Egypt [41].

9. Conclusion and Perspectives

The plants are used as medicines and foods widely in the world and for long time. The plants are very important for global health. The medicine and food dandelions have been widely used in folk with no adverse effects. The components, various effects and products have been reviewed derived from dandelions

in this article. The various effects including virus inhibition, anti-tumor activity, nutritional value, anti-aging, potential as a vaccine and alleviation of heat stress, seem scattered. The various effects are intrinsically related, and the mechanisms are intrinsically related.

It has been shown that dandelions inhibit many viruses and have anti-tumor activities, including GC, HCC, breast cancer, and uterine cancer. Dandelions also have high nutritional value and protect the liver to maintain normal nutritional metabolism. Dandelion extracts also inhibit aging and alleviate the adverse effects of heat, which is especially beneficial to the health of the aging population and people residing in extreme climates.

The mechanism underlying these effects of dandelions or other herbs is related to lncRNA, miRNA, DNA methylation, RNA editing, RNA polymerase, rDNA integrity and activity, and the methylation profile of DNA. Future in-depth research focuses on these effects of dandelions through RNA or DNA regulation. Based on the various effects, more foods and medical products may be developed from dandelions to increase the existing product categories.

Authors' Contributions

YY conceived and wrote the manuscript; CZ reviewed and approved the submitted manuscript; all authors read and approved the final manuscript.

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Availability of Data and Materials

All data and materials included in this article are available from the corresponding author upon request.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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Abbreviations

COVID-19: Coronavirus disease 2019;

EC: Endometrial carcinoma;

HCC: Hepatocellular Carcinoma;

lncRNA: Long non-coding RNA;

MEP: Methylerythritol 4-phosphate;

MVA: Mevalonate;

SRNAs: Small RNAs;

TQ: Toujie Quwen;

TCM: Traditional Chinese Medicine;

CCAT1: Transcript 1 associated with lncRNA colon cancer.