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Herbal Therapies for Prevention and Treatment of Influenza and Influenza-Like Illness

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Abstract

The frequent alterations in the antigenic structures of respiratory viruses make obstacles in the development of a novel vaccine or lead to ineffectiveness of an established one especially for RNA viruses. The unavailability of optimal medication and shortage of effective vaccines suggests the requirement for alternative therapies. Traditional herbal remedies were utilized by societies for prevention and treatment of viral respiratory illnesses. Several herbal extracts were proved effective on scientific bases such as maoto, licorice roots, antiwei, North American ginseng, berries, Echinacea, pomegranate, guava tea, and Bai Shao. The active ingredients of the plants (neuraminidase inhibitors, glycyrrhizin, polyphenol, baicalin) and the mechanism of action are well established. The herbal extracts could fight influenza by neuraminidase inhibition, preventing virus budding, assistance of viral bounding to natural antibodies, stimulation of IFN-gamma production by T cells, inhibition viral hemagglutination activity, inhibition viral binding to and penetration into host cells, enhancement production of anti-influenza virus immunoglobulin, synthesis inhibition of both viral RNA and protein, replication suppression of influenza virus, secretion induction of type I IFN and pro-inflammatory cytokines with subsequent stimulation of the antiviral activity, and exertion virion structural damage.

Keywords: Respiratory virus; Influenza treatment; Influenza prevention; Alternative therapy; Herbal medicine

Introduction

Respiratory viruses are a major cause of influenza-like illness (ILI) symptoms in children and adults, leading to substantial morbidity and mortality each year [1]. The frequent changes in the viral antigenic structure make difficulties in the development of vaccine especially for RNA viruses. Successfully manufactured vaccine could be less effective or ineffective when antigenic changes has developed in the target virus. Furthermore, during emergence of a newly virulent viral strain, production of a new vaccine requires time and might be unsuccessful. During the period between new virulent viral strain appearance and vaccine production, a lot of people might lose their lives as a result of influenza epidemic. Since there is no fully effective medication or vaccine for respiratory viral infections, therefore looking for alternative therapies is a reasonable requirement.

Herbal Therapies

Many herbal therapies were employed for prevention and treatment of viral respiratory illnesses. The herbal medicine, maoto, has been traditionally prescribed to patients with influenza in Japan. The administration of oral maoto granules to adults with seasonal influenza was well tolerated and associated with equivalent clinical and virological efficacy to neuraminidase inhibitors [2]. Maoto exerts antipyretic activity in influenza virus-infected mice and reduces virus through augmentation of the virus-bound natural antibodies [3]. Glycyrrhizin is an active component of licorice roots. It was investigated in mice infected with influenza virus A2 (H_2N_2) study revealed that glycyrrhizin might protect mice which were exposed to a lethal amount of influenza virus through the stimulation of IFN-gamma production by T cells [4]. Korean red ginseng (KRG) has become a popular influenza-like illness (ILI) medication in Korea. Predy et al. showed that the ginseng extracts decreased duration, severity, and frequency of symptoms of upper respiratory tract infections [5]. Ki-Chan et al. also demonstrated that the KRG extract can efficiently reduce the ILI incidence [6]. Antiwei, a traditional Chinese prescription in the treatment of influenza, was found effective and well tolerated in treatment of natural influenza infection in adults [7]. Another herbal product called COLD-fX (CVT-E002), a proprietary extract of the roots of North American ginseng (*Panax quinquefolius*). COLD-fX intake by immunocompetent elderly patients during an early cold and flu season reduced the relative risk and duration of respiratory symptoms by 48% and 55% respectively [8]. Elderberry intake also reduced the symptoms of influenza virus [9]. Extracts of berries inhibit influenza virus infection in vitro [10], and polyphenol is one of the key factors in the antiviral effects of berries [11]. Echinacea preparations are extensively used for the prevention and the management of the common cold. The preliminary results were encouraging, and suggest that Polinacea (roots of *Echinacea angustifolia*) could be used for improving the immune response to influenza vaccine [12]. In vitro test of the antiviral activities of *Thuja orientalis*, *Aster spathulifolius*, and *Pinus thunbergii* were examined. The three plant extracts were shown to induce a high cell viability rate after the infection with the influenza A/PR/8/34 virus. *Thuja orientalis* was found to have a stronger inhibitory effect than that with *Aster spathulifolius* or *Pinus thunbergii*. These results suggested that *T. orientalis* might be used for influenza treatment [13]. An aqueous-ethanolic extract of a mixture of *Thujae occidentalis herba*, *Baptisiae tinctoriae radix*, *Echinaceae purpureae radix* and *Echinaceae pallidae radix* were given orally for mice with Influenza A virus infection. The extract therapy induced a statistically significant increase in the survival rate, prolonged the mean survival time and reduced lung consolidation and virus titer. The study confirmed that

the plants mixture extract administration 6 days before exposure was a potent inhibitor of Influenza A virus in vivo [14]. *Clinacanthus siamensis* leaf extract showed activity in vitro and in vivo tests on influenza virus. After oral administration to mouse, the extract produced a higher anti-influenza virus IgG and IgA antibodies compared to oseltamivir [15]. *Punica granatum* (Pomegranate) had shown anti-influenza properties. Pomegranate polyphenol extract (PPE) was tested. It revealed replication suppression of influenza A virus in cell culture. PPE also prevented agglutination of chicken red blood cells by influenza virus, inhibited viral RNA replication, and was virucidal. In addition, the combination of PPE and oseltamivir synergistically had increased the anti-influenza effect of oseltamivir [16]. Electron microscopic analysis indicated that viral inactivation by pomegranates polyphenols was primarily a consequence of virion structural damage [17]. *Psidium guajava* Linn. (guava tea) had markedly inhibited the growth of clinical influenza A (H_1N_1) isolates. Guava tea inhibited viral hemagglutination and sialidase activity [18]. A plant known as *Epimedium koreanum* Nakai was extensively used in traditional Korean and Chinese medicine to treat a variety of diseases. It was effective against different influenza A subtypes by significant reduction in viral replication. The mechanism of antiviral activity was revealed where an aqueous extract from the plant induced the secretion of type I IFN and pro-inflammatory cytokines and the subsequent stimulation of the antiviral activity in cells [19]. A Chinese herbal known as *Scutellaria baicalensis* Georgi (baicalin), was used for the treatment of the common cold, fever and influenza virus infections. In cell culture and in mice baicalin revealed obvious antiviral activity that increased in a dose-dependent manner, indicating that baicalin affected virus budding. The investigators concluded that baicalin acts as a neuraminidase inhibitor, with distinct inhibitory activities that were effective against different strains of influenza A virus [20]. The root of *Paeonia lactiflora* Pall. (Bai Shao) a common chinese herb was employed in many recipes to treat viral infections and liver diseases. The synthesis of both viral RNA and protein was tremendously inhibited when the cells were treated with Bai Shao extract. The study demonstrated that the extract inhibits viral hemagglutination and viral binding to and penetration into host cells [21].

Conclusion

Several herbal therapies were proved to be effective for prevention or treatment of influenza and influenza like illnesses. The active antiviral substances were obtained by aqueous or ethanolic extracts of single or mixture of herbs. The effective plants were used traditionally in certain nations to treat respiratory viral infections. Maoto, licorice roots, Korean red ginseng, North American ginseng, antiwei, berries, Echinacea, pomegranate, guava tea, *Scutellaria baicalensis* Georgi, Bai Shao, and many other herbal extracts were found effective therapeutic agents. The mechanism of action is related to presence of substances in the herbs that prevent viral replication in human body. The identified active ingredients against respiratory viruses are neuraminidase inhibitors, glycyrrhizin (stimulating IFN-gamma production by T cells), polyphenol (causes virion structural damage) and baicalin (neuraminidase inhibitor).

References

1. Kaye M, Skidmore S, Osman H, Weinbren M, Warren R (2006) Surveillance of respiratory virus infections in adult hospital admissions using rapid methods. Epidemiol Infect 134: 792-798.
2. Nabeshima S, Kashiwagi K, Ajisaka K, Masui S, Takeoka H, et al. (2012) A randomized, controlled trial comparing traditional herbal medicine and neuraminidase inhibitors in the treatment of seasonal influenza. J Infect Chemother 18: 534-543.
3. Nagai T, Kataoka E, Aoki Y, Hokari R, Kiyohara H, et al. (2014) Alleviative Effects of a Kampo (a Japanese Herbal) Medicine "Maoto (Ma-Huang-Tang)" on the Early Phase of Influenza Virus Infection and Its Possible Mode of Action. Evid Based Complement Alternat Med 2014: 187036.
4. Utsunomiya T, Kobayashi M, Pollard RB, Suzuki F (1997) Glycyrrhizin, an active component of licorice roots, reduces morbidity and mortality of mice infected with lethal doses of influenza virus. Antimicrob Agents Chemother 41: 551-556.
5. Predy GN, Goel V, Lovlin R, Donner A, Stitt L, et al. (2005) Efficacy of an extract of North American ginseng containing poly-furanosyl-pyranosyl-saccharides for preventing upper respiratory tract infections: a randomized controlled trial. CMAJ, 173: 1043-1048.
6. Ha KC, Kim MG, Oh MR, Choi EK, Back HI, et al. (2012) A placebo-controlled trial of Korean red ginseng extract for preventing Influenza-like illness in healthy adults. BMC Complementary and Alternative Medicine 12: 10.
7. Wang L, Zhang RM, Liu GY, Wei BL, Wang Y, et al. (2010) Chinese herbs in treatment of influenza: A randomized, double-blind, placebo-controlled trial. Respiratory Medicine, 104: 1362-1369.
8. McElhaney JE, Goel V, Toane B, Hooten J, Shan JJ (2006) Efficacy of COLD-fX in the Prevention of Respiratory Symptoms in Community-Dwelling Adults: A Randomized, Double-Blinded, Placebo Controlled Trial. J Altern Complement Med 12: 153-157.
9. Rones ZZ, Thom E, Wollan T, Wadstein J (2004) Randomized study of the efficacy and safety of oral elderberry extract in the treatment of influenza A and B virus infections. J Int Med Res 32: 132-140.
10. Roschek B, Fink RC, McMichael MD, Li D, Alberte RS (2009) Elderberry flavonoids bind to and prevent H1N1 infection in vitro. Phytochemistry 70: 1255-1261.
11. Sekizawa H, Ikuta K, Mizuta K, Takechi S, Suzutani T (2013) Relationship between polyphenol content and anti-influenza viral effects of berries. J Sci Food Agric 93: 2239-2241.
12. Di Pierro F, Rapacioli G, Ferrara T, Togni S (2012) Use of a standardized extract from Echinacea angustifolia (Polinacea) for the prevention of respiratory tract infections. Altern Med Rev 17: 36-41.
13. Won JN, Lee SY, Song DS, Poo H (2013) Antiviral activity of the plant extracts from Thuja orientalis, Aster spathulifolius, and Pinus thunbergii against influenza virus A/PR/8/34. J Microbiol Biotechnol 23: 125-130.
14. Bodinet C, Mentel R, Wegner U, Lindequist U, Teuscher E, et al.(2002) Effect of oral application of an immunomodulating plant extract on Influenza virus type A infection in mice. Planta Med 68: 896-900.
15. Wirotesangthong M, Nagai T, Yamada H, Amnuoypol S, Mungmee C (2009) Effects of Clinacanthus siamensis leaf extract on influenza virus infection. Microbiol Immunol 53: 66-74.
16. Haidari M, Ali M, Ward Casscells S 3rd, Madjid M (2009) Pomegranate (Punica granatum) purified polyphenol extract inhibits influenza virus and has a synergistic effect with oseltamivir. Phytomedicine 16: 1127-1136.
17. Sundararajan A, Ganapathy R, Huan L, Dunlap JR, Webby RJ, et al. (2010) Influenza virus variation in susceptibility to inactivation by pomegranate polyphenols is determined by envelope glycoproteins. Antiviral Res 88: 1-9.
18. Sriwilaijaroen N, Fukumoto S, Kumagai K, Hiramatsu H, Odagiri T et al. (2012) Antiviral effects of Psidium guajava Linn. (guava) tea on the growth of clinical isolated H1N1 viruses: its role in viral hemagglutination and neuraminidase inhibition. Antiviral Res 94: 139-146.
19. Cho WK, Weeratunga P, Lee BH, Park JS, Kim CJ, et al. (2015) Epimedium koreanum Nakai displays broad spectrum of antiviral activity in vitro and in vivo by inducing cellular antiviral state. Viruses 7: 352-377.

20. Ding Y, Dou J, Teng Z, Yu J, Wang T, et al. (2014) Antiviral activity of baicalin against influenza A (H1N1/H3N2) virus in cell culture and in mice and its inhibition of neuraminidase. Arch Virol 159: 3269-3278.

21. Ho JY, Chang HW, Lin CF, Liu CJ, et al. (2014) Characterization of the anti-influenza activity of the Chinese herbal plant Paeonia lactiflora. Viruses 6: 1861-1875.