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Short Communication

A new alternative to treat swine influenza A virus infection: extracts from *Terminalia chebula* Retz.

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Currently, a pandemic swine influenza A virus infection causes a huge negative impact on human beings all over the world. However, the methods of treatment are not satisfactory, therefore it is urgent for us to set up new theory and practice to fight against the intractable virus. *Terminalia chebula Retz*, as a kind of traditional Chinese medicine, widely distributes and has multiple pharmacological effects. Evidences in laboratory and clinic practice confirm us to the potential of *Terminalia chebula Retz* inhibiting influenza A virus infection. We thus hypothesize that acetone extracts (tannic acids, A) of *Terminalia chebula Ret* may as a new alternative treat influenza A infection based on holistic concept of traditional Chinese medicine principle.

Key words: Swine influenza A virus, *Terminalia chebula* Retz, hypothesis.

INTRODUCTION

Beginning in March 2009, an outbreak of influenza A (Family Orthomyxoviridae, Genus Influenzavirus A) has become the greatest pandemic disease threat to humankind [Neumann et al., 2009]. The new strain of influenza virus designated Influenza H1N1 2009, is a reassortant of swine, avian and human influenza viruses [Brown, 2000; Olsen, 2002; Webby et al., 2000]. Although the influenza A infection has less mortality, compared with other companions such as HIV-1, Ebola, SARS, the current transmit will not stop until pandemic eventually involve 80 percent of population all over the world according to WHO report.

At present there are only two classes of antiviral drugs are approved to treat against influenza viruses including adamantanes and neuraminidase inhibitors such oseltamivir and zanamivir [Schnitzler and Schnitzler, 2009]. However, the effect of viral chemo-therapy that applies a single compound is limited with side effect such as diarrhea, dizziness or insomnia and this kind of therapy may cause drug resistant. *Terminaliae immaturus*, the fruitlet of *Terminalia chebula Fructus Retz*, which has been given the name of XiQingGuo, mainly distribute in Malaysia, Thailand, India, Pakistan and Yunnan, Tibet, Guangdong, Guangxi province of China [Saleem et al., 2001; Kusirisin et al., 2009; Nariya et al., 2009; Cai et al., 2008].

Its active components which refer to acetone extracts (TA) contain digallic acid, chebulinic acid, chebulagic acid, terchebin and gallic acid with multiple pharmacologic actions such as anti-virus, anti-oxidation, cardiotonic action, antibacterial effect, anti-anaphylaxis, anti-tumor growth, [Saleem et al., 2001; Kusirisin et al., 2009; Nariya et al., 2009; Cai et al., 2008; Feng et al., 2008; Kusirisin et al., 2009; Murali et al., 2007; Lee et al., 2007; Lee et al., 2005; Juang et al., 2004; Saleem et al., 2002; Malekzadeh et al., 2001; Sato et al., 1997; Verma and Raychaudhuri, 1970; Cheng et al., 2003]. Those biological activities are often in connec-tion with the high contents of tannic acids [Kim et al., 2009].

THE HYPOTHESIS

To sum up the above statements, it is wise for us to get help from nature and from ethnopharmacological record

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or traditional medicine principle handed down from ancient times all over the world to battle with current pandemic influenza A virus. We will use acetone to extract from *Terminalia chebula* Retz to get a tannic acid mixture to inhibit pandemic influenza A infection.

The theory of our hypothesis

As we all know the influenza virus subtypes have a wide host range from avian to mammals including hens, pigs, horses and dogs. The genomes of influenza A virus are segmented and negative-sense RNAs which can be translated into 11 functional proteins [Schnitzler and Schnitzler, 2009; Fitzgerald, 2009; Gatherer, 2009]. The main infective proteins contain the surface glycoproteins haemagglutinin (HA) binding virus to its purposive target cell, neuraminidase (NA) facilitating virus release from infected cells and virulence factors NS1 antagonizing host interferon. There are 16 serotypes of haemagglutinin, and 9 serotypes of neuraminidase in total and according to these differences, the virus are classified. Sialic acid is the receptor for haemagglutinin and sialyltransferases is expressed in human mucosal and respiretory tissues resulting in N-glycans with α-2,6 linked sialic acids. However in avian tissues, another structure of sialic acid is expressed and N-glycans are linked with α-2,3-sialic acid. These different structures lead to virus specifying hosts, e.g. avian viruses mainly infect bird species. Like other RNA viruses, e.g. hepatitis C virus and HIV, influenza virus is characterized by genetic variability, resulting in frequent mutations and reassortment on account of influenza virus RNA polymerase lack of proofreading abilities [Reid and Taubenberger, 2003]. Thus the genetic material of current pandemic influenza A H1N1 virus is a combination of viruses that have infected pigs, birds and humans respecting swine tissues express both forms of sialic acid and can be coinfected with human and avian viruses [Olsen, 2002].

It is reported that the rate of oseltamivir-resistant human seasonal H1N1 in the USA has increased to 98.5% [Poland et al., 2009], up from 10% in the last year. Although the instances of appearance of current pandemic influenza A H1N1 virus resistant to oseltamivir in Denmark, Japan and Hong Kong are only sporadic cases, the outbreak of large scale cases will happen inevitably if no effective actions are taken on. In addition, the supply with antiviral drugs is not sufficient for a pandemic and the cost of drugs is too expensive to afford especially for the developing countries.

Another alternative to defend virus infection is to appeal to our own immune system. On way the infected host immune system counters viral infection is with interferon, one of the principle functions of which is to interfere with viral multiplication without affecting the host cell itself.

Interferons, a group of small proteins, produced by virus-infected cells, react with plasma or nuclear membrane receptors of uninfected cells to induce synthesis of antiviral proteins. Antiviral proteins are possessed of multiple functions to prevent further infection of virus including blocking initiation of virus protein synthesis, inhibiting virus polypeptide elongation and destroying viral mRNA before translation. Even through there do exists problems partially due to short term effectiveness of interferon, it typically plays a positive role against acute and short term virus infection especially influenza. Therefore any measures that could improve our immune system response to secret sufficient interferon are suggested and approved.

In laboratory test, the water decoction of *Fructus terminaliae immaturus* exhibit obvious antibacterial effect inhibiting both Gram positive bacterium including *Staphylococcus aureus, Pneumococcus, Streptococcus hemolyticus, Bacillus diphtheriae* and Gram negative bacterium including *Escherichia coli, Bacillus dysenteriae, Pseudomonas aeruginosa, Bacillus proteus, Bacillus tphpi, Bacillus typhi murium, Helicobacter pylori.* The alcoholic extracts of *Terminalia chebula Retz* demonstrated significant anti-virus effect in 2.2.15 cell line infected with HBV, and the extracts with a certain concentration of hydrochloric acid have a more powerful inhibitory effect on bacterium and fungus growth. Chinese patent medicines containing *Terminalia chebula Retz* can inhibit acyclovir-resistant herpes simplex virus I *in vitro and in vivo*. In addition, in animal research, *Terminalia chebula Retz* was used to treat endotoxin sepsis shock because *Terminalia chebula Retz* can regulate immune response by making host cells release interferon and TNF as well as activating monocyte/macrophage system [Cai et al., 2008; Feng et al., 2008].

Feasibility and prospects

We will use acetone to extract from *Terminalia chebula* Retz to get a tannic acid mixture without purification further. Base on traditional Chinese medicine and Chinese materia medica principle, we would like to emphasize the holistic concept, which means that every thing should be considered as a whole and there is synergistic effect of each component of a plant. The synergy is not the simple sum of several components, but rather mutually reinforcing role, with a single component can not be achieved. The aim of extraction is not intended to find a single anti-viral compound, but rather to remove impurities to enhance antiviral activity of *Terminalia chebula Retz* according to guiding role of holistic concept. The extracts combined with pandemic influenza A virus were inoculated into nonimmune chick embryo, and then the chick embryo and allantoic fluid were observed to evaluate the antiviral effect of the extracts.

RESULTS

Natural medicine of the antiviral and enhancing immunity

including extract or mixture, which may fight against influenza virus through different targets.

CONCLUSION

The acetone extract (tannic acids, TA) of *Terminalia chebula Ret* may be considered as a effective method for human being fighting against pandemic swine influenza A virus on account of its low cost, easy preparation and significant therapeutic action.

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