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Effect of Curcumin and Artemisinin - Future Perspective on COVID-19

Dr. M. Shanthi[1], Dr. R. Raju Ganesh[2]

Department of Oral Medicine and Radiology, SRM Kattankulathur Dental College and Hospital, SRM University, Potheri, Tamilnadu, India

Emergency Medicine

Abstract: ***The coronavirus disease (COVID-19) has been declared as a worldwide pandemic by the world health organization. This coronavirus disease was detected in late December 2019 and recognized in early January 2020 in China. On 11 February 2020, the international committee stated that "severe acute respiratory syndrome coronavirus 2" (SARS-CoV-2) as the new deadly virus. The COVID-19 spread abruptly across the globe, becoming a pandemic within a couple of weeks and apart from China, affecting countries like the USA, Italy, Spain, France, Germany, Iran and India. Several attempts have been made in the research and development of the diagnostics, therapeutics and vaccines for coronavirus, but no chemotherapeutic agent has found which has been shown effective in treating against this virus. This review will be compiling the antiviral activity of herbal plants curcumin and artemisinin against the virus***

Keywords: coronavirus disease (COVID-19), Middle East Respiratory Syndrome (MERS), Severe Acute Respiratory Syndrome (SARS)

1. Introduction

A Corona virus comes under large family of viruses. It affects both humans and animals. Seven different types of corona viruses can produce infection in people around the worldbut commonly people get infected with these four human type of viruses: 229E, NL63, OC43, and HKU1. It causes a respiratory infection ranging from the common cold to more severe diseases such as Middle East Respiratory Syndrome (MERS) and Severe Acute Respiratory Syndrome (SARS) and the most recently discovered corona virus (COVID-19) that causes more deadly infectious disease.[1] The standard tool of diagnosis is by reverse transcription polymerase chain reaction (rRT-PCR) from a throat swab ornasopharyngeal swab. The infection can also be diagnosed from a combination of symptoms, risk factors and a chest CT scan showing features of pneumonia.

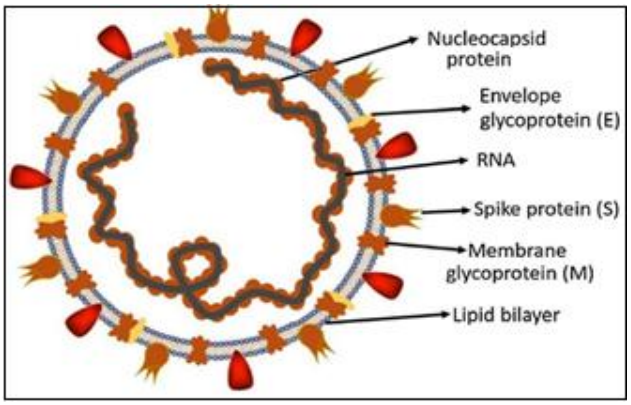

Figure 1: A structure of Respiratory Syndrome (SARS) coronavirus

Other thanSARS-CoV-2, there are six known coronaviruses in humans: HCoV-229E, HCoV-OC43, SARS-CoV, HCoVNL63, HCoV-HKU1, and MERS-CoV.

Curcumin

It was first isolated in 1815, while its chemical structure was determined in 1973 by Roughley and Whiting .[1]It as an antioxidant, anti-inflammatory, and anti-atherosclerotic.[2]

It is the principle component of turmeric, an edible component through different parts of Asia, for its flavor, color and medicinal properties. In Ayurveda, curcumin is used as treat for a variety of health conditions, including respiratory illness, liver disorders, inflammatory disorders and diabetic wounds.

According to the Goel et al evidences suggest that curcumin is a highly pleiotropic molecule with numerous targets and mechanisms of action. It has properties thatalter the activity of enzymes, growth factor receptors, cofactors, and other molecules.[3]Curcumin (diferuloylmethane) is the principal curcuminoid of the turmeric, and the other two are demethoxycurcumin and bis-demethoxycurcumin. Turmeric (C. longa) is a plant native to India and Indonesia. Its tuberous rhizomes (root-like structures) have been in use, since ages, as a condiment, spice, food preservative, dye, aromatic stimulant, and as an auspicious material in various Hindu rituals.[(4-7).]

Curcumin can exist in at least two tautomeric forms, ketoand enol. The enol form is more energetically stable in the solidphase as well as in solution. The enol form can also cross the
blood–brain barrier[8]

Antiviral Activity of Curcumin

I. Dairaku et al stated that the Inosine monophosphate dehydrogenase (IMPDH) enzyme due to rate-limiting activity in the *de novo* synthesis of guanine nucleotides is suggested as a therapeutic target for antiviral and anticancer compounds. 15 different polyphenols of curcumin has inhibitory activity against IMPDH effect in either noncompetitive or competitive manner is suggested as a potent antiviral compound.[9] Viral long terminal repeat

(LTR) has a critical role in Transcription of type 1 human immunodeficiency virus (HIV-1) provirus. Inhibition of LTR activity can be a possible pathway for antiviral drug candidates in order to block HIV-1 replication. Curcumin proved to be an effective compound to inhibit the HIV-1 LTR-directed gene expression[(10-11)]. It also inhibits the acetylation of Tat protein of HIV significantly by p300 associated with suppression of HIV-1 multiplication.

James et al conducted a study in which he stated that curcumin as an anti-HIV compound in 40 patients in eight weeks and it was shown that there is no reduction in viral load or elevation in CD4 counts. But patients claimed that they preferred to take the curcumin in order to tolerate the minor gastrointestinal sufferings.[12]A study was conducted which proved that clear liquid soap containing 0.5% w/v ethanol extract of *C. longa* rhizome on HIV patients reduced the wound infections and 100% decrease in itching symptom and it also affected the abscess to convert to dryness scabs (78.6%) within 2 weeks. Some studies have stated that it has anti-influenza activity against influenza viruses PR8, H1N1, and H6N1 and 90% reduction in virus yield in cell culture using30 μM of curcumin.[13.]

According to k.zandi et al gallium-curcumin and Cu-curcumin, showed antiviral activity against herpes simplex virus type 1(HSV-1) in cell culture with IC50 values of 33.0 microg/mL, 13.9 microg/mL, and 23.1 microg/mL.it also decreased the immediate early (IE) gene expression and infectivity of HSV-1 in cell culture assays.[14]K.Z Bourne et al conducted a study on a mouse model intravaginal HSV-2 challenge showed significant protection against HSV-2 infection due to administration of curcumin.[15]X. Si et al stated that the curcumin exhibited the antiviral activity against coxsackie virus by reduction of viral RNA expression, protein synthesis, and virus titer and it was also found to have a protective effect on cells against virus induced apoptosis and cytopathic activity and Analysis was also done in different pathways and showed that it forces its potent antiviral effect in inhibition of coxsackievirus replication through dysregulation of the ubiquitin-proteasome system.[16]

The study of antiviral effect of aqueous extract of *Curcuma longer* hizoma against HBV in HepG cells containing HBV genomes showed repression of HBsAg secretion from liver cells without any cytotoxic effect. It also suppressed the HBV particles production and the rate of mRNA production of HBV on infected cells. Curcumin showed the inhibitory activity against the expression of E6and E7 genes of HPV-16 and HPV-18 as two main highlyoncogenic human papilloma viruses. Japanese encephalitis virus (JEV) as an important endemicarbovirus in Southeast Asia is a major cause of acute enceph alopathy which generally affects the children. The investigation of antiviral activity of curcumin on Neuro2a cell line infected with JEV showed reduction in production of infectious viral particles through inhibition of ubiquitin-proteasomesystem.[16]

According to the Sordillo et al the suppression of multiple cytokines by curcumin suggested that it can be a useful to treat Ebola patients against cytokine storm .[17]In the study by Mazumder et al stated that curcumin inhibited HIV replication. The specific interaction of curcumin with the viral proteins integrase and protease, which play central roles in viral replication, might represent the underlying mechanism for this effect and Kutluay et al. also reported that curcumin treatment inhibited herpes simplex virus.[18]

ARTEMISININ

Artemisinins called as sweet wormwood (or sweet Annie: Artemisia annua). They were first discovered, ‘‘qinghao’’ extracts were reported to have antipyretic properties more than 1500 years ago.[19]In 1972, it was isolated for the first time from a Chinese medicinal plant, *Artemisia annua*(an herbaceous plant of the family *Asteraceae*), and is a sesquiterpene lactone natural product. Since the discovery of the antimalarial activity of Artemisinin and its semi-synthetic derivatives, they have been used in the treatment of malaria as first-line drugs. Its derivatives are dihydroartemisinin (DHA), artemether, arteether, and artesunate.

Antiviral Activity of Artemisinin

It can be easily purified by crystallisation after extraction from Artemisiaannua plants but is extremely difficult to synthesise de novo. It does not dissolve in oil or water and so can only be given by the enteral route.

Chinese scientists stated that artemisinin might have antiviral activity [20]. Artesunate inhibits the invitro replication of HCMV and herpes simplex virus type 1 (HSV-1)[21]. Artesunate is also effective against clinicalisolates of HCMV and mutants with resistance against conventionalantiviral drugs, such as ganciclovir and cidofovir. Herpesviruses from all subfamilies (a, b, and g) are also sensitive to artesunate—namely, Epstein-Barr virus, herpes simplex virus 1, and human herpes virus . This indicates that the semisynthetic drug artesunate has more antiherpesviral potencythan does its natural parental drug, artemisinin.[22]

Birku et al. investigated the effect of artemisinin on the rate of clearance of *Plasmodium falciparum* in patients with or without HIVcoinfection.[23]

2. Conclusion

Curcumin is bioactive compound against different diseases but it also have a major flaw to use it in the field is its deliverymechanisms.The optimum potential of curcumin is limited because ofpoor oral bioavailability and insufficient solubility in aqueoussolvents leading to poor absorption, fast metabolism, andquick systemic elimination. Since artemisinin is known as a gold standard for antimalarial, it also has few antiviral properties. More research and clinical trials are required for curcumin and artemisinin and its derivative as antiviral for prevention and treatment of new emerging coronavirus.

References

[1] WHO Q&A on coronaviruses (COVID-19) March 2020, https://www.who.int/news-room/q-a-detail/q-a-coronaviruses

[2] Araujo CA, Leon LL. Biological activities of *Curcuma longa* L. *Mem. Inst. Oswaldo Cruz, Rio de Janeiro.* 2000, 96, 723–728.
[3] Beevers CS, Huang S. Pharmacological and clinical properties of curcumin. *Biol. Targets Ther*. 2011, 1, 5–18.
[4] Goel A, Kunnumakkara AB, Aggarwal BB. Curcumin as "Curecumin": fromkitchen to clinic. BiochemPharmacol. 2007
[5] Lim GP, Chu T, Yang F, Beech W, Frautschy SA, Cole GM. The curry spice curcumin reduces oxidative damage and amyloid pathology in an Alzheimer transgenic mouse. J Neurosci. 2001;21:8370–7.
[6] Mishra S, Palanivelu K. The effect of curcumin (turmeric) on Alzheimer's disease: an overview. Ann Indian Acad Neurol. 2008;11(1):13–9.
[7] Kohli K, Ali J, Ansari MJ, Raheman Z. Curcumin: a natural antiinflammatory agent. Indian J Pharmacol. 2005;37(3):141–7.
[8] Akram M, Shahab-Uddin AA, Usmanghani K, Hannan A, Mohiuddin E, Asif M. Curcuma longa and curcumin: a review article. Rom J Biol Plant Biol. 2010;55:65–70
[9] Kolev TM, Velcheva EA, Stemboliyska BA, Spiteller M. DFT and experimental studies of the structure and vibrational spectra of curcumin Int J Qua Chem. 2005;102:1069–79
[10] I. Dairaku, Y. Han, N. Yanaka, and N. Kato, "Inhibitory effect of curcumin on IMP dehydrogenase, the target for anticancer and antiviral chemotherapy agents, " *Bioscience, Biotechnology and Biochemistry*, vol. 74, no. 1, pp. 185–187, 2010.
[11] G. J. Nabel, S. A. Rice, D.M. Knipe, and D. Baltimore, "Alternative mechamisms for activation of human immunodeficiency virus enhancer in T cells, " *Science*, vol. 239, no. 4845, pp. 1299–1302, 1988.
[12] B. R. Cullen and W. C.Greene, "Regulatory pathways governing HIV-1 replication, " *Cell*, vol. 58, no. 3, pp. 423–426, 1989.
[13] J. S. James, "Curcumin: clinical trial finds no antiviral effect, " *AIDS Treatment News*, no. 242, pp. 1–2, 1996.
[14] D.-Y. Chen, J.-H. Shien, L. Tiley et al., "Curcumin inhibits influenza virus infection and haemagglutination activity, " *Food Chemistry*, vol. 119, no. 4, pp. 1346–1351, 2010.
[15] K. Zandi, E. Ramedani, K. Mohammadi et al., "Evaluation of antiviral activities of curcumin derivatives against HSV-1 in Vero cell line, " *Natural Product Communications*, vol. 5, no. 12, pp. 1935–1938, 2010
[16] K. Z. Bourne, N. Bourne, S. F. Reising, and L. R. Stanberry, "Plant products as topical microbicide candidates: assessment of *in vitro* and *in vivo* activity against herpes simplex virus type 2, " *Antiviral Research*, vol. 42, no. 3, pp. 219–226, 1999.
[17] X. Si, B.M.McManus, J. Zhang et al., "Pyrrolidine dithiocarbamate reduces coxsackievirus B3 replication through inhibition of the ubiquitin-proteasome pathway, " *Journal of Virology*, vol.79, no. 13, pp. 8014–8023, 2005.
[18] Sordillo, P.P.; Helson, L. Curcumin Suppression of Cytokine Release and Cytokine Storm. A Potential Therapy for Patients with Ebola and Other Severe Viral Infections. In Vivo **2015**, 29, 1–4.
[19] Sordillo, P.P.; Helson, L. Curcumin Suppression of Cytokine Release and Cytokine Storm. A Potential Therapy for Patients with Ebola and Other Severe Viral Infections. In Vivo **2015**, 29, 1–4.
[20] Qinghaosu Antimalaria Coordinating Research Group. Antimalaria studies on Qinghaosu. Chin Med J (Engl) 1979;92:811–16.
[21] Qian RS, Li ZL, Yu JL, Ma DJ. The immunologic and antiviral effect of qinghaosu. J Tradit Chin Med **1982**; 2:271–6.
[22] Efferth T, Marschall M, Wang X, et al. Antiviral activity of artesunate towards wild-type, recombinant, and ganciclovir-resistant human cytomegaloviruses. J Mol Med **2002**; 80:233–42.
[23] Naesens L, Bonnafous P, Agut H, De Clercq E. Antiviral activity of diverse classes of broad-acting agents and natural compounts in HHV- 6–infected lymphoblasts. J Clin Virol**2006**; 37(Suppl 1):S69–75.
[24] Birku Y, Mekonnen E, Bjorkman A, Wolday D. Delayed clearance of *Plasmodium falciparum* in patients with human immunodeficiency virus co-infection treated with artemisinin. Ethiop Med J **2002**; 40:17–26.