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# CURCUMIN: A RAY HOPE AS PREVENTIVE MEASURES FOR COVID 19 INFECTION

**Nikita M. Shevkar[*1], Ramesh A. Gadekar[2], Ashwini V. Shelke[3] and Anil G. Jadhav[4]**

[1]Department of Quality Assurance, Sandip Institute of Pharmaceutical Science, Nashik, Maharashtra, Postal Code-422213.

[2]Department of Pharmaceutics, Sinhgad Technical Education Society's, Smt.Kashibai Navale College of Pharmacy, Kondhwa Budruk, Kondhawa-Saswad Road, Pune-411048.

***Corresponding Author: Nikita M. Shevkar**

Department of Quality Assurance, Sandip Institute of Pharmaceutical Science, Nashik, Maharashtra, Postal Code-422213.

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## ABSTRACT

Novel COVID-19 is a virus-related syndrome that occurs as a result of severe acute respiratory syndrome coronavirus-2. The family of coronavirus is coronaviridae family. This disease was invented from Wuhan city of Hubei region in China, in December 2019 and it is range in over 210 countries in world. Coronavirus is a single stranded, positive sense RNA virus and it is transmitted to human via respiratory droplets. The patients show the flu like signs with a dry cough, sore throat, sneezing, lethargy, muscle pain, high fever and breathing problems.

Till Now a days there is not any particular treatment is available for Covid-19 disease. Some combination of antiviral agents such as Hydroxylchloroquine and Azithromycin are used as supportive treatment for covid-19 disease. However Unani, Homeopathy and Ayurveda therapy may be used along with Allopathic therapy. This article probably focuses on the Ayurveda therapy as supportive treatment in covid-19 disease. A curcumin is a natural, herbal,polyphenolic constituent which obtained from roots of the rhizome plant *curcuma longa* belongs to family *Zingiberaceae*, is shows a potential effects in covid-19 disease.

We briefly summarize potential effects of the curcumin in the cure of the covid-19 in this review.

**KEYWORDS**- Covid-19, Curcumin, Coronavirus, Infection, Disease.

## INTRODUCTION

Novel covid-19 is an epidemiologic disease occurs due to coronavirus which is belonging to family *coronaviridae* and appears just similar to sharp rings while saw under electron microscope. The surface appearances by means of several spikes, which are useful to attack and bind to the living cells. These viruses are having a constructive sense single stranded RNA genome and helical symmetry nucleocapsid.The coronavirus causes simple common cold illness to severe illness like severe acute respiratory syndrome.[1, 2]Typically, the size of coronavirus are of ~20 nm and arranged with outsized petal surface appearance. The initial coronavirus was revealed in 1937 in birds and far ahead on in the 1960 in human. The structure of coronavirus is shown in fig.1.

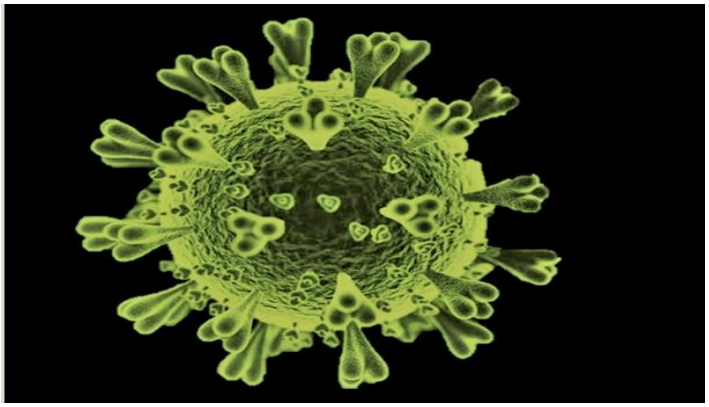

**Figure: 1. Structure of coronavirus.**

It is essential to comment that the 2019-2020 outbreak of novel coronavirus is started in Wuhan, Hubei region of China in December 2019,[3] when a novel straining of coronavirus was identified on 31st December 2019.[4] The World health organization takes certain forename to this virus as 2019-nCov.[5] Which was later give new name by means of the international committee on taxonomy of virues as severe acute respiratory syndrome coronavirus 2 (SARs-Cov-2). The disease triggered through this virus is known as as coronavirus disease 2019 and shortened as Covid-19. [CO: corona, VI: virus, D: disease and 19: 2019 year.[6-8]

Coronavirus infect the upper gastrointestinal and respiratory tract in mammals (Includes humans) and the birds. The complete medical description of the covid-19 is not fully recognized. The event of infection ranged as of mild to severe. The symptoms of covid-19 may arise within 2-14 days after the infection.[9] The common symptoms of the infection are tiredness, sore throat, muscle pain, sneezing,, dry cough, elevated fever, respiratory problem etc. with certain severe causes having pneumonia, severe respiratory syndrome, kidney failure and even death.[10-12] The covid-19 possibility is more in elder peoples, kids and the patients having others health problem like lungs disease, heart disease, diabetes and cancer. The spreading of coronavirus is occurs by the sneezing, cough drops and contact. Normally this virus come into the body by way of the mouth, nose and eyes.[13]

Till a date there is no particular antiviral treatment is available to treat covid-19, only a supportive treatment is used in covid-19 disease, includes allopathic homeopathy and ayurvedic. In Ayurveda, a curcumin is natural, polyphenolic composite take out from the *curcuma longa* belongs to family *zingiberaceace*. Several studies reported that curcumin has beneficial effects in treating cardiovascular disease, metabolic syndrome and viral disease. It has prominent results in treating a covid-19.[14]

**Curcumin as antiviral agent and role of curcumin in coronavirus infection**

Curcumin is a natural, polyphenolic constituent obtained from the plant curcuma longa belonging to the family zingiberaceace that has long history to be used in humans in treating disease without overt side effects. Numerous in vivo and in vitro studies indicates that curcumin has antioxidant, anti-inflammatory, anticancer and antidiabetic activity.[15] Several clinical studies documented that the curcumin has beneficial effects in treating cardiovascular disease, metabolic disease or diabetes, infectious diseases specially viral infections.[16] Curcumin disrupts the virus-related infection progression by the use of several mechanism such as directly targeting viral proteins, inhibiting particle production and virus entry, replication and budding.[17] A newly in vitro study has shown that curcumin hinders respiratory syndrome virus (RSV) by obstructing attachment to host cells.[18]

Furthermore, curcumin,act against SAR-CoV ,According a study going on the anti-SAR-CoV activity of 221 phytocompunds revealed that 20 µM of curcumin exhibit important inhibitory sound effects in a Vero E6 cell-based cytopathogenic effect(CPE) assay. The authors presented evidence for a mild effect of curcumin in contrast to SAR-CoV replication and the inhibitory properties of curcumin on SAR-CoV 3CL protease activity, which is essential for the replication of SARs-CoV.This study provides promising evidence for cucumin as potential anti-SARs-CoV agent. The picture of curcumin is shown in figure.

**Figure. 2: picture of curcumin.**

In last two decades, coronavirus infection has gained much attaintion for its high mortility.[19] The consensus from recent research is that the cytokine storm shows an essential role in the growth and progress of lethal pneumonia. Targeting cytokine storm is reflected as an important strategy for Cove infection. Among individuals who experienced SARs-Cove infection in 2003, lots of showed ALI and established ADRs, and the death rate was greater than 10%.[20] Similar conditions are seen in MERS-CoV, H5N9, H7N9 and SARs-CoV 2 infection. Currently, no clinical data in human on the relation among curcumin and coronavirus infection have

been available, but in lesser and its preventive and healing character in pathological infection, courcumin can possibly measure as a smart agent for the managing of coronavirus.[21]

**Curcumin can potentially target steps of viral Replication cycle**

For replication of virus they require enzyme and the virus do not be necessary all the enzyme which is required for replication as single unit. With the help of cellular machinery metabolic progressions and reproduction takes place. The replication of viruses includes, attachment, penetration, uncoating, genome replication, and gene expression are possible therapeutic targets.[22] A common effect of curcumin involves imminent viral infections by targeting permeation of virus and attacking the components essential for viral reproduction.[23]

**Viral attachment/penetration**

On application of curcumin to cells prior or subsequent to infection, it decrease infectivity of some viruses. Du et al. estimate the effect of curcumin on the entry of virus. The Curcumin blocks the entry of viruses to cell by changing the surface of protein structure in viruses. The positively charged curcumin on the exterior of protein structure is exposed to electrostatic interactions with plasma membranes and incompatible with virus to bind with cells.[24] ACE2 receptor that binds with SARSCoV-2 spike glycoprotein which enables membrane fusion and viral infection take place through endocytosis. Therefore, spike glycoprotein is a possible applicant for drug targeting to prevent the approach of virus that in silico docking studies discovered that curcumin can possibly inhibit ACE2 to suppress COVID19 entry to the cell.[25,26]

**Viral replication**

For inhibiting the virus one of the probable therapeutic approaches is using agents that can possibly inhibit the reproduction of virus. Wen et al. have studied the effect of curcumin on viral replication by quantification of the number of spike proteins present in cultures of Vero E6 cells infected with SARS-CoV. Their end result shows that the values of inhibitory effect of curcumin in EC50 was more than 10 μM on SARS-CoV replication.[27] Furthermore, Ting Du et al. studied the sound effects of curcumin on negative-strand RNA synthesis by means of PEDV as a coronavirus model. They proven that curcumin may possibly inhibit PEDV at the replication phase. The numbers of plaque were reduced when exposed to curcumin. The reduction in plaque numbers and virus titers signify that curcumin could inhibit viral replication. This proof supports the probable role of curcumin as a likely antiviral agent.[28, 29]

**Effect of curcumin on Interferons**

Interferon's play vital role in defense against Covid 19 infection. The virus can hamper the installation of interferon in humans. The virus antagonizes STAT1, which is a key protein in the interferon-mediated immune response.[30] It shows the increased immune cell response entrance to IFNs at the time of these infections All IFNs is most important for prevention of viral infections. The elevated death rates in elderly people could be understood by the higher interferon mediated immune response entry. For reducing death due to SARA-Cove the activation of natural immune responses to trigger IFN production at the very early stages of this disease.[31] Can achieve by administering agents that could elevate the synthesis of IFNs like poly ICLC. Still the appropriate dosing and most favorable timing for such interventions need to be confirmed in clinical trials even though we have positive conclusions of pre-clinical studies on the potency of IFNs in treating CoV-induced infections,. Moreover, IFN-I as well as IFN-γ therapy both together is strongly recommended There is increase in positive results day by day on the impact of curcumin on IFNs in various viral diseases. To produce several antiviral cytokines the viruses can Stimulate interferon-regulatory factors and NF-κB. The synthesis of a diverse IFN-stimulated genes (ISGs) is persuaded by the antiviral IFNs via the JAK/STAT pathway.[32,33] To freeze various stages of viral replication the IFN-independent pathways are directly stimulated by antiviral IFNs Ting Du et al. have shown that decrease in the PEDV model of coronavirus reproduction is observed when treated with cationic carbon dots based on curcumin and this is done by stimulating the production of interferon-stimulating genes (ISGs) and the cytokines (IL8 and IL6) of Vero cells by triggering the innate immunity of the host.[34]

**Effect of curcumin on pulmonary inflammation, fibrosis, edema-Pulmonary inflammation-**

Curcumin blocks crucial signals that regulates expression of varoi pro-inflammatory cytokines comprises of nuclear factor-κB and MAPK pathways. Curcumin is having anti-inflammatory as well as antifibrotic effects by decreasing expression of essential chemokine's and cytokines include in lung infection like IFNγ, MCP-1, IL-6, and IL-10.[35, 36]

**Pulmonary fibrosis**

It is a destructive result of COVID-19 infection connected to acute respiratory distress syndrome (ARDS) in around 32% patients which are infected with COVID-19. When SARS-CoV-2 affect both the lower and upper respiratory tract, produces variety of ARDS, releasing pro-inflammatory cytokines.[37] When SARS-CoV-2 attached to toll-like receptor, pro-IL-1β is release and it is split by caspase-1, which leads to activation of inflammasome and generation of active mature IL-1β, which intervenes pulmonary inflammation and fibrosis. Curcumin inhibit cellular inflammatory response by reducing the cytokine/chemokine expression via NF-κB pathway and fibrotic response during regeneration phase of the disease through reducing TGF-ß pathway in a mouse model of viral-induced ARDS.[38]

**Pulmonary oedema**

When some of the patients with COVID -19 were examined they showed pulmonary oedema together with inflammatory a cluster which consists of fibrinoid material and multinucleated giant cells.[39] In the pulmonary oedema accretion of fluid in lungs occurs the activation of protein kinase C by SARS-CoV envelope (E) Protein the activation of protein kinase C occurs which results in the decrease activity of epithelial sodium channels at apical surface of pulmonary epithelial cells, and the ion channel activity of E protein leads to pulmonary oedema.[40]

**Effect of curcumin in the treatment of covid19 associated cardiovascular damage**

Angiotensin-converting enzyme 2 (ACE2) is an enzyme having cardiovascular function and also involved for developing hypertension, diabetes mellitus. When virus spike protein binds to ACE2, SARS-CoV-2 infection starts.[41, 42] SARS-CoV-2 causes respiratory symptoms by infecting alveolar epithelial cells. These symptoms are mostly observed in patients suffering from cardiovascular disease. It is because of fact that patients having cardiovascular disease, the ACE2 expressed increased as compared with peoples who do not have.[43, 44] As ACE2 decreases it will be harmful to heart, which causes dysfunction, partly because of increased stimulation of AT1 receptor by angiotensin II.

In patients with COVID-19 infection, cardiovascular symptoms arise due to systemic inflammatory response triggered by disproportionate feedback of type 1 and type 2 T helper cells.[45, 46]

**Effect of curcumin in covid-19 associated with kidney damage**

Due to SARSCoV-2 the incidence of acute kidney injury increases, death rate is increased as patient having acute renal injury. ACE2 is mostly expressed in the kidneys. As there is depletion in ACE2 and increasing in ACE expression that results as renal damage in in the patients with diabetes. ACE inhibitors may have some adverse effects in managing COVID-19 infection.[47,48] Curcumin can stimulate ACE2 mRNA and ACE2, which results in enhancement of renal blood flow. At priming and activation stages Curcumin lessens the renal fibrosis by suppressing the inflammation because of decrease MCP-1, NF-κB, TNF-α, IL-1β, COX-2, and Cav-1.[49,50]

## CONCLUSION

In this review article, potential effects of curcumin on SARSCoV-2 infection are being discussed. The curcumin is able to regulate broad range of molecular targets, and also having advantageous effects against COVID-19 infection that's why curcumin used to manage coronavirus infection. Curcumim is having capability to regulate the varying molecular targets and also regulate cellular signaling pathways like pulmonary edema inflammation, RNA replication. Apoptosis in COVID-19 infection can also suppress by the use of curcumin. The curcumin is mainly used against various diseases as it is having potential effects, safety profile, but due to the restricted bioavailability of turmeric, problematic issue are created by oral administration .Yang et al. reveal that when curcumin is given intravenously (10 mg/kg) then it will shows better bioavailability when compared with oral administration with increased dose (500 mg/kg). In the various clinical trials it is observe that by administering high concentrations of curcumim with non-toxic limit the alleviated bioavailability observed. The curcumin is having the immunomodulatory, anti-inflammatory effects along with anti-fibrotic effect and the pulmonoprotective effects on lung tissue, so curcumin is mainly used to treat COVID-19. For both prevention and treatment of coronavirus curcumin is helpful which is having antiviral and anti-inflammatory agent. Although, proper clinical trials are required to reveal the potential effectiveness of curcumin to act in opposition to SARS-CoV-2 infection.

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**CONFLICT OF INTEREST-** None.

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