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Can guggul cure COVID-19 ?

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Abstract
Pandemic COVID-19, may be one among the greatest tragedy of 21st Century. It has brought social and economical unrest across the continents. Research are on fast track on finding a remedy to check CoVID-19 in various research institutions. Amidst these developments we would like to open an another window of possibility and that is can we consider Guggul gum. In the present review we have tried to focus the therapeutic and medicinal properties of guggul gum, keeping in mind COVID-19.

Keywords: Corona virus, Herbal medicine, Natural products, Oleo-resin, Respiratory tract, Symptoms

Introduction
Corona viruses (CoVs) are the member of RNA viruses with ability to infect both human and animals (Ye *et al*., 2020). Respiratory system is one of the vital systems it infects, besides gastro intestinal and central nervous system (Cui *et al*., 2019) [9]. The outbreak of severe acute respiratory syndrome corona virus (SARS-CoV) and Middle East respiratory syndrome corona virus (MERS-CoV) proved deadly (Ramadan and Shaib, 2019) [45] as thousands lost their lives (Mubarak *et al*., 2019) in the past two decades. In a sharp contrast to these epidemics, the outbreak of highly contagious CoVID-19 is pandemic (WHO, 2020), that spread from Wuhan, China (Huang *et al*., 2020) [15] to the world at large. Therapies like viral and corticosteroids as well as mechanical respiratory support is being tried to contain this infection but a specific treatment for COVID-19 is yet to happen (Huang *et al*., 2020) [15].
Lin *et al*., (2014) [27] have summarized several natural products and herbal medicines against some notable viral pathogens including corona virus (CoV), coxsackie virus (CV), dengue virus (DENV), entero virus 71 (EV71), hepatitis B virus (HBV), hepatitis C virus (HCV), herpes simplex virus(HSV), human immune deficiency virus (HIV), influenza virus, measles virus (MV), and respiratory syncytial virus (RSV).

1. Symptoms of CoVID-19
The symptoms of COVID-19 infection though appear after an incubation period of approximately 5.2 days (Li *et al*., 2020) [68], but days to death range from 6 to 41 days with a median of 14 days (Wang *et al*., 2020) [64, 65]. It all depends on the age and immune system of the patient, as it was shorter among patients over 70-years old (Wang *et al*., 2020) [64, 65]. Fever, cough and fatigue are the most common symptoms of COVID-19 while other symptoms include sputum production, headache, haemoptysis, diarrhoea, dyspnoea, and lymphopenia (Ren *et al*., 2020; Huang *et al*., 2020; Lu, 2020) [47, 15, 31, 32, 33]. Clinical features revealed presence of pneumonia, acute respiratory distress syndrome, acute cardiac injury and incidence of grand glass opacities that led to death (Huang *et al*., 2020) [15]. Multiple peripheral ground glass opacities were observed in subpleural regions of both lungs (Lei *et al*., 2020) [25] in some cases it is a cause of increased inflammation. Regrettably, treatment of some cases with interferon inhalation showed no clinical effect and instead appeared to worsen the condition by progressing pulmonary opacities (Lei *et al*., 2020) [25]. Fever, dry cough, dyspnea, and bilateral ground-glass opacities on chest CT scans are a few common symptoms of both COVID-19 and betacoronavirus (Huang *et al*., 2020) [15]. However, targeting of the lower airway as evident by upper respiratory tract symptoms like rhinorrhoea, sneezing, and sore throat are unique clinical features of COVID-19 reported by Assiri (2013) [13]. Phan *et al*., (2020) [42] observed an infiltration in the upper lobe of the lung that is associated with increasing dyspnea with hypoxemia of chest radiograph of COVID-19 patients. In comparison to the MERS-CoV or SARS-CoV patients, Gastro-intestinal symptoms like diarrhoea were observed in higher percentage of COVID-19 patients (Assiri, 2013) [13].

2. Causal organism

CoVs have become the major causal organisms or pathogens of respiratory disease outbreaks. They are a large family of single-stranded RNA viruses (+ssRNA) that can be isolated in different animal species (Perlman and Netland, 2009). For reasons yet to be explained, these viruses can cross species barriers to cause in humans, illness ranging from the common cold to more severe diseases such as MERS and SARS. The probable origins of latter two viruses are may be from bats (Cui *et al*., 2019) [9] and their transmission into mammalian hosts before humans.

World Health Organisation (WHO) has classified COVID-19 as a β CoV of group 2B (Hui *et al*., 2020) [16]. Ten genome sequences of COVID-19 obtained from nine patients exhibited 99.98 percent sequence identity (Lu *et al*., 2020) [31, 32, 33]. In an another study of five patients there was 99.8 to 99.9 percent nucleotide identity in isolates and the sequence too revealed presence of a new β-CoV strain (Ren *et al*., 2020) [47].

3. COVID-19 origin

Genetic sequence study of COVID- 19 revealed that it had over 80 and 50 percent similarity in SARS-CoV and MERS-CoV respectively (Ren *et al*., 2020: Lu *et al*., 2020) [47, 31, 32, 33]. Thus, the evidence from the phylogenetic analysis indicates that the COVID-19 belongs to the genus β-CoV strain. This strain includes SARS-CoV, that infects humans, bats, and wild animals (Zhu *et al*., 2020) [71]. COVID-19 represents the seventh member of the coronavirus family that infects humans and has been classified under the ortho-coronavirinae subfamily. The COVID-19 forms a clade within the subgenus sarbecovirus (Zhu *et al*., 2020) [71].

Existence of a high degree of homology of the Angiotensin converting enzyme 2 (ACE2) receptor from a diversity of animal species, implicates them as possible intermediate hosts or animal models for COVID-19 infections (Wan *et al*., 2020) [63]. Moreover, CoV viruses have a single intact open reading frame on gene 8, which is a further indicator of its bat-origin CoVs. The amino acid sequence of the tentative receptor-binding domain resembles that of SARS-CoV, indicating that these viruses might use the same receptor (Ren *et al*., 2020) [47].

4. Nature of damage

Patients with hypertension, diabetes, coronary heart disease, cerebro-vascular illness, chronic obstructive pulmonary disease, and kidney dysfunction are susceptible and have worse clinical outcomes when infected with SARS-CoV-2. Existence of significantly increased fibrin degradation products (FDPs) and reduced platelets in severe COVID-19 patients is consistent with the presence of hyper-fibrinolysis. Plasmin is a key player in fibrinolysis as it enhances the virulence and pathogenicity of viruses. Presence of haemorrhage in multiple organs and a positive correlation between fibrinolysis and mortality is an important observation.

In the early stages of COVID-19 infection, Tian *et al*. (2020) [61] observed presence of pneumonia, oedema, proteinaceous exudate with globules and focal hyperplasia of alveolar epithelial cells associated with patchy inflammatory infiltrates and multi-nucleated giant cells in thepuncture lung biopsies. At the later stages of infection, diffuse alveolar damage (DAD) in addition to haemorrhage and some areas of interstitial fibrosis was observed by Luo *et al*., 2020. Presence of fibrotic clots and gelatinous mucous in the small airways and disseminated intravascular coagulation were other observations recorded by Liu *et al*., (2020) [28, 29, 30]. Lungs are the most injured organs, followed by moderate injury in the heart, liver, kidney and brain in COVID-19 patients. Systemic micro-thrombi in the circulatory system and haemorrhage in the affected organs results from non-coordinated responses between the coagulation and fibrinolysis systems.

Some COVID-19 patients showed higher leukocyte numbers, abnormal respiration and increased levels of plasma pro-inflammatory cytokines. The positive real-time polymerase chain reaction (RT-PCR) of sputum of a COVID-19 patient with 5 days of fever of 39.0 °C accompanied cough, coarse breathing sounds of both lungs confirmed COVID-19 infection (Lei *et al*., 2020) [25]. Further they observed Leucopenia with leukocyte counts of 2.91 × 10^9 cells/L of which 70.0% were neutrophils; blood C-reactive protein value of 16.16 mg/L above the normal range of 0–10 mg/L blood; high erythrocyte sedimentation rate and D-dimer.

Huang *et al*., 2020 [15] after clinical study of COVID-19 patients admitted in intensive care unit revealed severe pneumonia combined with the incidence of ground-glass opacities acute cardiac injury with high blood levels of cytokines and chemokines (IL1-β, IL1RA, IL7, IL8, IL9, IL10, basic FGF2, GCSF, GMCSF, IFNγ, IP10, MCP1, MIP1α, MIP1β, PDGFB, TNFα, and VEGFA). High levels of pro-inflammatory cytokines (IL2, IL7, IL10, GCSF, IP10, MCP1, MIP1α, and TNFα) that are reasoned to promote disease severity.

5. Molecular pathway

Nucleotide sequences of hundreds of SARS-CoV-2 virus isolates revealed a close relation to two bat-derived corona viruses, bat-SL-CoVZC45 and bat-SL-CoVZXC21. These corona virus strains have a similar receptor-binding domain structure in the Spike (S) protein for host angiotensin converting enzyme 2 (ACE2) proteins (Lu *et al*., 2020; Zhou *et al*., 2020) [70, 31, 32, 33]. The S protein of SARS-CoV-2 binds to human ACE2 receptors with higher affinity than that of the SARS-CoV virus (Wrapp *et al*., 2020) [66]. This may be due to a furin-like cleavage site (^{682}RRAR/S^{686}) inserted in the S1/S2 protease cleavage site of the SARS-CoV-2 virus (Coutard *et al*., 2020) [8].

The S1 region of the Spike protein is responsible for binding to the host cell ACE2 receptor, where the S2 region is responsible for fusion of the viral RNA and cellular membranes. Polybasic furin sites in hem-agglutinin (HA) proteins are often found in highly virulent avian and human influenza viruses. The insertion of the furin site may augment the ability of this new SARS-CoV-2 to attach and invade human cells expressing ACE2 and CD147 receptors (Wang *et al*., 2020) [64, 65].

Usually, β CoV produce a ~800 kDa polypeptide upon transcription of the genome. This polypeptide is proteolytically cleaved to generate various proteins. The proteolytic processing is mediated by papain-like protease (PLpro) and 3-chymotrypsin-like protease (3CLpro). The 3CLpro cleaves the polyprotein at 11 distinct sites to generate various non-structural proteins that are important for viral replication (Anand *et al*., 2003) [2].

Thus, 3CLpro play a critical role in the replication of virus particles and unlike structural/accessory protein-encoding genes, it is located at the 3' end which exhibits excessive variability.

6. Possible strategic intervention points

Currently no clinically proven specific anti-viral agent is available for SARS-CoV-2 infection, except the supportive treatment, oxygen therapy, conservation fluid management, and broad-spectrum antibiotics to cover secondary bacterial infection (Huang *et al*., 2020) [15]. According to the research on molecular mechanisms of corona virus infection (Groneberg *et al*., 2004) [14] and the genomic organization of SARS-CoV-2 (Lu *et al*., 2020) [31, 32, 33], there are several potential therapeutic targets to repurpose the existing antiviral agents or develop effective interventions against this novel corona virus. Non-structural proteins like 3CLpro and PLP, have an essential function for coronaviral replication and can inhibit the host innate immune responses (Chen *et al*., 2020) [5, 6]. Thus 3CLpro inhibitors - such as and flavonoids (Jo *et al*., 2020) [19], while PLP inhibitors - like diarylheptanoids, are possible intervention points to fight against SARS-CoV-2. ACE2 mediates SARS-CoV-2 entry into the cell as a functional receptor of corona viruses. Blocking the binding of S protein with ACE2 can also be another strategic intervention against SARS-CoV-2 infection (Li *et al*., 2005) [26].

a. Guggul -an oleo-resin gum as a natural product for possible intervention against SARS-CoV-2 infection

At this point, it is worth introducing Guggul -an oleo-resin gum as a natural product for possible intervention against SARS-CoV-2 infection. Guggul is an exudate of *Commiphora wightii* (Arnott.) Bhandari, having medicinal importance with proven array of health-promoting properties (Siddiqui, 2011) [54]. Therapeutic role of guggul against diverse chronic diseases such as *viz*., Alzheimer's disease, arthritis, cancer, pancreatitis, IBD, dermatitis, diabetes, infectious diseases, intestinal metaplasia, otitis media, respiratory disease and asthma etc. besides its anti-inflammatory and anti-oxidant properties is well documented (Kunnumakkara *et al*., 2018) [24].

b. Bio- active compounds of guggul

Naringenin, one of the many biologically active compounds of guggul is well known to prevent the accumulation of lipoproteins and also acts as anti-bacterial, anti-inflammatory, anti-viral agent (Kay, 1996) [21]. Ellagic acid is another bio-active compound present in guggul posessing antiviral properties (Thresiamma *et al*., 1996) [60].

Guggul is a complex mixture of steroids, amino acids, carbohydrates, aliphatic esters, diterpenoids, and different inorgranic compounds. Cholestrol and sesamin has been isolated (Dev. 1983) [12]. E-Guggulsterone, Z-Guggulsterone, Guggulsterol I, Guggulsterol II, Guggulsterol III, Guggulsterol IV and Guggulsterol-V are also isolated (Purushothaman and Chandrasekaran, 1976) [44]. Beside these steroid compounds, mukulol an alcoholic compound has also been isolated (Bajaj and Sukh, 1982) [4].

Table 1: Therapeutic value of guggul

1	E-Guggulsterone and Z-Guggulsterone has hypolipidemic properties (Macha *et al*., 2010) [35].
2	Naringenin prevents the accumulation of lipo-proteins and possess anti-bacterial, anti-inflammatory, anti-viral properties (Kay 1996) [21].
3	Cembranoids controls the gastro-intestinal absorption of cholesterol and fat (Yu *et al*., 2009) [69].
4	Myrrhanol i.e. triterpenoid of guggul gum acts that as anti-inflammatory and also reduce pain in osteo arthritis patients (Kimura *et al*., 2001) [22].
5	Eugenol (mono terpenoid) having the anti-oxidant and anti-microbial properties also plays a vital role in the cell proliferation in tumors (Nagababu and Lakshmaiah, 1992) [39].
6	Quercetin has most effective inducer effect for the anti-carcinogenic (Manjeet and Ghosh, 1999) [36] activity.
7	Diayangambin having the immunomodulatory and anti-inflammatory properties is used to reduce the ear swelling (De Leon *et al*., 2002) [10].
8	Ellagic acid has anti-mutagen, anti-inflammatory and anti-cancer properties (Thresiamma *et al*., 1996) [60]. It binds with cancer cells and makes them inactive.
9	Mansumbinoic acid also acts as anti-inflammatory and anti-bacterial agent (Duwiejua *et al*., 1993) [13].
10	Alpha terpineol has strong anti-microbial properties (Park *et al*., 2012) [41].
11	1, 8-cineole acts as anti-inflammatory and anti-nociceptive (Santos and Rao, 2002) agent.

Extracts of guggul oleo gum resin contain compounds which are known for their hypolipidemic activity.Main reported compounds are E-Guggulsterone, Z-Guggulsterone and other guggulsterone compounds. Other constituents of guggul are Guggul tetrols, Octadecane-1,2,3,4-tetrol, non adecan-1,2,3,4-tetraols,terpenes and lignans i.e.. Guggullignan I, Guggullignan II, ferulic acid and sesamin (Singh *et al*., 1990; Satyavati, 1969) [55, 51]. Myrcene 3.50%, Alpha-pinene 4.75%, Methyl chavicol 5.40%, 1,8-cineole (eucalyptol)-3.5% are the essential oil compounds found in guggul.

Thus goes the list of uses of guggul apart from numerous life-threatening diseases such as bone fracture, arthritis, cardiovascular diseases, and obesity (Tomer *et al*., 2014) [62] as well as anti-cancerous, anti-malarial, anthelmintic and anti-dysenteric properties (Sharma and Kumar, 2012) [52]. Guggul is used for lacquer, incense sticks, varnishes and ointments (Rout *et al*., 2012) [49]. Santhal tribes use its bark for treating ulcers, for curing pyorrhea, bronchial asthma and as mosquito repellent (Tomer *et al*., 2014). Dysmenorrhea, dyspepsia, endometriosis, hypercholesterolemia, hypertension, impotence, mania, rheumatism, sores, leprosy, leukoderma, anemia and occlusion etc. (Rout *et al*., 2012) [49] are other therapeutic uses of guggul. It has conjointly been reported as anti-schistosomal, hepato-protective, muscle relaxing, larvicidal, in diarrhea, cough and chest ailments (Kulloli and Kumar, 2013) [23]. Poonia *et al*., (2014) [43] and Tomer *et al*., (2014) reported guggul as its thyroid stimulant, antiseptic, astringent, carminative, diaphoretic, demulcent, emmenagogue, sedative and diuretic.

c. Anti-inflammatory

Inflammation is commonly associated with an elevated production of cytokines and chemokines, while guggul causes a reduction in the pro-inflammatory cytokines. TNF-α, IL-1β, IL-6, and IL-8, and an elevation in the level of anti-inflammatory cytokine IL-10 (Mohan *et al*., 2019) [38].

Table 2: Nuclear Factor kappa-light-chain-enhancer of activated B cells (NF- *κ*B)

1	NF-*κ*B is a transcription factor playing a central role in the regulation of diverse cellular processes including inflammation, immune response, differentiation, proliferation, and apoptosis.
2	Activation of NF-kB can be achieved by induction with pro-inflammatory molecules, such as tumor necrosis factor *α* (TNF-*α*), interleukin-1*β* (IL-1*β*), and phorbol myristate acetate (PMA).
3	A number of NF-*κ*B target genes have a primarily inflammatory function, such as monocyte chemotactic protein (MCP)-1, regulated upon activation normal T-cell expressed and secreted protein (RANTES), interleukin-1 (IL-8), C-X-C motif ligands (CXCLs), and C-C motif ligand 20 (CCL20). Thus, it becomes obvious that NF-*κ*B is a critical regulator for inflammatory responses.
4	Under the resting condition, NF-*κ*B is associated with an inhibitory subunit of NF-*κ*B (I*κ*B) in cytoplasm.
5	Upon stimulation by various agents, I*κ*B is phosphorylated by I*κ*B kinase (IKK) for ubiquitin-dependent degradation, leading to nuclear translocation of NF-*κ*B and activation of NF-*κ*B target genes. Recent studies have demonstrated that guggulsterone inhibits NF-*κ*B activation induced by a variety of agents in several cell types (Shishodia and Aggarwal 2004; Ichikawa and Aggarwal 2006) [53, 17].
6	Such repression of NF-*κ*B activation is mediated through a direct inhibition of IKK activation by guggulsterone (Shishodia and Aggarwal 2004) [53]. Recent study revealed that repression of NF-*κ*B activation through inhibition of IKK activity represents a mechanism of the anti-inflammatory effect of guggulsterone. This proposed mechanism is supported by the results from another study in which guggulsterone blocked the NF-*κ*B signaling pathway by targeting IKK complex (Cheon *et al*. 2006) [7].

Guggulsterone has been found to be a potent inhibitor of the nuclear factor-*κ*B (NF-*κ*B) (Shishodia and Aggarwal 2004; Ichikawa and Aggarwal 2006; Cheon *et al*. 2006) [53, 17, 7], a key regulator for inflammatory responses. Such repression of NF-*κ*B activation may represent a mechanism for the anti-inflammatory effect of guggulsterone.

To better understand the role of guggulsterone on cytokine induced inflammation, Lu *et al*. (2008) [34] studied the effect of guggulsterone on IL-1β- and IFN-γ-induced beta-cell damage in the islets of Langerhans. Treatment of rat insulinoma cells with IL-1β and IFN-γ induced cell damage, which correlated with nitric oxide (NO) and prostaglandin E2 (PGE2) production. Guggulsterone completely prevented cytokine mediated cytotoxicity, as well as NO and PGE2 production. Guggulsterone suppressed levels of inducible nitric oxide synthase (iNOS) and cyclo-oxygenase (COX)-2 mRNA and protein expression, most likely through suppression of NF-κB. The cytoprotective effects of guggulsterone were also mediated through suppression of the JAK/STAT pathway. Levels of the protein SOCS-3 were down-regulated in cells treated with the cytokines. Collectively, these results suggest that guggulsterone prevented cytokine-induced cell damage (Lu *et al*.2008) [34].

High-sensitivity C-reactive protein (hs-CRP), an acute-phase reactant mainly synthesized in the liver in response to the cytokine stimulation, is an index of inflammation (Jialal *et al*. 2004) [18]. Clinical trial conducted in the United States, demonstrated that the median serum hs-CRP level was decreased (Szapary *et al*. 2003) [57, 58], indicating the anti-inflammatory activity of guggul.

Cyclo-oxygenase 2. COX-2 converts arachidonic acid into prostaglandins and prostanoids. COX-2 induction is responsible for inflammation and pain. It is demonstrated that guggulsterone suppressed TNF-induced *COX-2* promoter activity and protein expression *in vitro* in a dose-dependent manner (Shishodia and Aggarwal, 2004) [53]. As already noted, guggulsterone suppressed cytokine-induced expression of *COX-2* mRNA and protein in rat insulinoma cells (Lu *et al. 2008*) [34].

Nitric oxide synthase (iNOS). iNOS is one of three key enzymes generating NO from the amino acid L-arginine. Meselhy, (2003) [37] found guggulsterone to inhibit lipo-polysaccharide-induced NO production in macrophages. While Lu *et al*. (2008) [34] observed guggulsterone suppressing cytokine-induced expression of *iNOS* mRNA and protein. These observations suggest that guggulsterone may have anti-metastatic activity through suppression of iNOS.

d. Anti-oxidant

Cytokine storm is generally observed in both viral and bacterial infections (Teijaro, 2017) [59] resulting an increased oxidative stress via a common and non-specific pathway. Since the prevention and management of oxidative stress may be done with the application of anti-oxidants and this approach may be applicable to COVID-19. Antioxidant effect of guggul and guggulsterone has been demonstrated *in vitro* and *in vivo* (Kaul and Kapoor, 1989) [20]. Xanthine oxidase - an enzyme that promotes the production of reactive oxygen species, whereas super xide dismutase (SOD) is an important antioxidant enzyme catalyzing the conversion of superoxide anion to oxygen and hydrogen peroxide. Guggulsterone reverse both isoproterenol-induced production of xanthine oxidase and isoproterenol-mediated decrease of superoxide dismutase. Guggulsterone inhibits the production of toxic oxygen free radicals. The antioxidant activity of guggulsterone was reported by Singh *et al*. (1994; 1997) [56]. It is generally accepted that overproduction of nitric oxide is associated with oxidative stress, which is involved in the pathogenesis of cardiovascular diseases, diabetes, rheumatoid arthritis, neurodegenerative diseases, or chronic inflammation (Moncada *et al*. 1991) [39]. In one of the study, guggulsterone isomers (Z- and E-forms) exhibited potent inhibitory activity against the production of nitric oxide induced by bacterial lipopolysaccharides (Meselhy 2003) [37]. This finding indicated that guggulsterone may be of therapeutic benefit in diseases associated with oxidative stress.

e. Fibrinolysis

Guggul promotes fibrinolysis (dissolving the fibrin in blood clots) and act as an antioxidant. Guggulsterones support in platelet functioning, fibrinolytic activity and also maintain cardiovascular activities (Deng, 2007) [11]. Study on the effect of guggul on fibrinolysis and platelet adhesiveness in coronary heart disease revealed that fibrinolytic activity increased, while the platelet adhesive index decreased (Bordia and Chuttani, 1979), which indicates that guggul may be a useful therapeutic agent in the management of COVID-19.

f. Immunomodulator

An immunomodulator can be defined as a substance, which can influence any constituent or function of the immune system in a specific or nonspecific manner including either innate or adaptive arms of the immune response (Agrawal and Singh 1999) [1]. Guggul possess immunomodulator properties as it provides support to immune fractions, improves the defense mechanism of body (Rao *et al*., 1994) [46]. When virus

is inhaled and infects respiratory epithelial cells, dendritic cells phagocytose the virus and present antigens to T cells. Effectors T cell functions by killing the infected epithelial cells, and cytotoxic CD8+ T cells produce and release pro-inflammatory cytokines which induce cell apoptosis (Rogers and Williams, 2018) [48]. Both the pathogen (CoV) and cell apoptosis trigger and amplify the immune response. The exacerbation of cytokine production, excessive recruitment of immune cells and the uncontrollable epithelial damage generates a vicious circle for infection related ALI/ARDS (Yang *et al*., 2018) [67]. The clinical characteristics of COVID-19 suggest that a reduced level of neutrophils, lymphocytes and CD8+ T cells in peripheral blood (Chen *et al*., 2020; Liu *et al*., 2020) [5, 6, 28, 29, 30].

Table 3: Guggul as a natural product in management of COVID-19

1	The symptoms of COVID-19 explained in context to therapeutic properties of guggul gum, the possible management strategy can be better analyzed.
2	Guggul:
3	Promotes fibrinolysis, platelet functioning and also maintain cardiovascular activities.
4	A potent inhibitor of the nuclear factor-*κ*B (NF-*κ*B) a key regulator for inflammatory responses. Repression of NF-*κ*B activation may represent a mechanism for the antiinflammatory effect of guggel.
5	Inhibits isoproterenol-induced production of xanthine oxidase which promotes the production of reactive oxygen species.
6	Inhibits the production of toxic oxygen free radicals.
7	The bioactive compound Naringenin prevents the accumulation of lipoproteins and also presents anti-bacterial, anti-inflammatory, anti-viral properties.
8	Possess immunomodulator properties as it provides support to immune fractions, improves the defense mechanism of body.

g. Experience with Jawahar Guggul Laddu

Jawaharlal Nehru Krishi Vishwa Vidyalaya, Jabalpur formulated Jawahar Guggul Laddu (FSSAI Lic No. 21418170000805). JGL is prepared with pure natural Guggul, Linseed (flaxseed), Rajgira and Honey. Each 20g JGL contains 10mg guggul. The permissible mean daily intake (MDI) of pure guggul is 10mg but for severe diseases it can be increased upto 1000mg (Szapary *et al*., 2003) [57, 58]. We suggest to take on JGL daily, early morning in empty stomach for general health. Our regular customers of JGL have shared their experience of reduction of blood sugar and joint pain, correction of thyroid, gastrointestinal pain. In view of experience of JGL and the medicinal benefits of guggul gum, the pharmacologist may try to develop a product for curing COVID-19 patients in near future.

Declarations of interest: none.

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