The role of gum Arabic as an anti-inflammatory, antioxidant, and immune modulator in COVID-19: A review

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ABSTRACT

Background: Down-regulation of the lung inflammatory response seems to preserve pulmonary functions and improve survival in COVID-19. The key factor in overcoming the cytokine storm caused by COVID-19 by immunomodulation, rather than immunosuppression. Identifying the right mechanism to manipulate the immune regulatory networks in the lung—with minimal side effects—represents one of the many challenges in the treatment of COVID-19 disease. Immunomodulatory, anti-inflammatory, antioxidant, and gut-regulatory activities are the most significant properties of prebiotics. Therefore, it could be beneficial to consider them as an adjuvant dietary intervention among COVID-19 patients. Understanding the exact mechanism of prebiotic defense against infection and regulation of immune processes involved in COVID-19 are crucial for the development of novel therapeutic agents. Several studies considered Gum Arabic (GA) as a potent prebiotic with cytoprotective properties. This review aims to discuss and display the possibility of utilizing the beneficial effects of GA to modulate COVID-19 pathogenesis.

Keywords: COVID-19, Gum Arabic, Immunomodulation, dietary intervention, Gut microbiota, Anti-inflammatory, Antioxidant
INTRODUCTION In the first quarter of 2020, the World Health Organization (WHO) declared the pandemic COVID-19 outbreak. Several trials for COVID-19 treatment have been conducted. The world expects to experience many waves of COVID-19 outbreaks with the lifting of restrictions and lockdowns, and herd immunity is still far away to be achieved (1).

Mild COVID-19 affects healthy individuals leading to seasonal, slight to moderate cold flu-like symptoms affecting the upper respiratory tract. In contrast to the highly pathogenic virus, SARS-CoV-2 infects causes severe pneumonia, and acute respiratory distress syndrome (ARDS) (2). The main cause of death is ARDS and multiple organ failure is secondary to the cytokine storm (CS) (3). Inflammation is the key pathogenesis in COVID-19 patients (4) since the severity of ALI (Acute Lung Injury) was accompanied by an elevated expression of inflammation-related genes rather than increased viral titers (4). As a result, finding a way to block the CS using anti-inflammation therapy is critical for lowering COVID-19-related mortality (5).

The discovery of COVID-19 RNA in the stool of patients and the presence of diarrhea as one of the clinical symptoms proposed a link between the lung and the intestine (6). Gut microbiota was found to tune the immune system and balance the pro and anti-inflammatory response (7), can suppress viral infection and prevent immune over-reaction that can be destructive to lung and vital organ systems (8).

Gum Arabic (GA) is a natural exudate from Acacia Senegal and/or Acacia seyal trees (9-11). It is considered a safe additive dietary fiber since the 1970s, approved by FDA and JECFA (12). The chemical structure is composed mainly of polysaccharides with galactopyranosyl residues (11), which are rich in calcium, zinc, magnesium, and potassium salts (11). In addition to a small portion (about 10%), is a protein content corresponding to a complex Arabinogalactan-Protein (13).

Gum Arabic is widely used in physiological and pharmacological research as an experimental vehicle for drugs (13). GA exhibited strong anti-inflammatory, antioxidant, anti-microbial, and immunomodulatory effects in several studies in vivo and in vitro experiments.
We review the evidence showing that GA has the potential to support adjuvant efficacy in treating COVID-19-induced lung injury and acute respiratory distress syndrome secondary to COVID-19 infection, as well as provide a theoretical basis for GA application among COVID-19 patients as adjuvant and supportive therapy.

**Table 1.** Summarized Antioxidant, Anti-inflammatory and Immuno-Modulatory Effect of Gum Arabic on Vivo and Vitro Experimental Studies

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<th>Title</th>
<th>Biological Activities</th>
<th>Dose and Duration</th>
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| Acacia Senegal gum exudate offers protection against cyclophosphamide-induced urinary bladder cytotoxicity (24) | GA revealed a significant recovery in the bladder by:
- Increase response to Ach
- 23% drop in bladder weight (edema)
- Decrease NO content to control level.
- Increase Glutathione (GSH) to control level.
- Decrease Malondialdehyde (MDA) to control level.
- Improvement of histological changes. | 7.5 g/kg/day for 6 days | vivo | Male Swiss Albino Rats | 21 |
| Ameliorative Effect of Gum Acacia on Hookah Smoke-Induced Testicular Impairment in Mice (25) | Increase Testosterone
Increase Estradiol
Increase luteinizing hormone
Decrease Androgen binding protein
Decrease Urine Cotinine
Glutathione
Total nitrite
Decrease Plasma inhibin B
Decrease Plasma of lactate dehydrogenase (LDH)
Decrease Alkaline phosphatase
No effect Lipopolysaccharide binding protein
Decrease Uric acid
Decrease 8-oxo-2' deoxyguanosine
Decrease Cytochrome C
Decrease Malondialdehyde (MDA)
Decrease Nuclear factor-κB (NF-κB)
Decrease Nuclear factor erythroid 2–related factor 2 (Nrf2)
Decrease Interleukin-6 (IL-6)
Decrease Interleukin-1β (IL-1β)
Decrease Transforming growth factor-β1 (TGF-β1)
Decrease Tumor necrosis factor-α (TNFα).
Normal superoxide dismutase (SOD) expression in germ cells | 15%, w/v, in the drinking water for 30 days | vivo | Male Mice | 22 |
| Antimicrobial and Immunomodulatory Effect of Gum Arabic on Human and Bovine Granulocytes Against Staphylococcus aureus and Escherichia coli (27) | GA exhibiting a direct antibacterial effect on pathogenic S. aureus isolates.
Increase oxidative burst/ROS production of bovine and human granulocytes in a dose-dependent manner,
Increase NO and ROS production,
No effect was seen on neutrophil extracellular trap (NET), | 5%,10%, 20% (w/v) | vitro & vivo | Bacteria, isolated primary blood-derived granulocytes | 23 |
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<tr>
<td>Antioxidant effect of Arabic gum against mercuric chloride-induced nephrotoxicity (28)</td>
<td>• GA reversal of (mercury) Hg-induced increase in creatinine, blood urea nitrogen, thiobarbituric acid reactive substances, and total nitrate/nitrite to control values,&lt;br&gt;• Prevented Hg-induced degenerative changes of kidney tissues.</td>
<td>7.5 g/kg/day for 5 days per oral administration</td>
<td>vivo</td>
<td>Rats</td>
<td>24</td>
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<tr>
<td>Effect of Gum Arabic on Oxidative Stress and Inflammation in Adenine–Induced Chronic Renal Failure in Rats (30)</td>
<td>• Decrease TNF-a concentration in urine and plasma.&lt;br&gt;• Increase Anti-inflammatory cytokine IL-10 significantly increased in the GA-treated rats.&lt;br&gt;• Decrease superoxide production to control levels.&lt;br&gt;• Decrease DNA double-strand breaks.&lt;br&gt;• Increase glutathione (GSH) concentration,&lt;br&gt;• Increase superoxide dismutase (SOD) activity&lt;br&gt;• Increase Total antioxidant activity (TAOA) in plasma.</td>
<td>(15%, w/v) for 4 weeks</td>
<td>vivo</td>
<td>Rats</td>
<td>26</td>
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<td>Effect of Gum Arabic (Acacia Senegal) on C-reactive protein level among sickle cell anemia patients (19)</td>
<td>Decrease C-reactive protein (CRP),</td>
<td>30 g/day for 12 weeks</td>
<td>vivo</td>
<td>Human (sickle cell anemia patients)</td>
<td>16</td>
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<td>Gum Arabic as novel antioxidant agent in sickle cell anemia, phase II trial (29)</td>
<td>• Increase TAC (total antioxidant capacity),&lt;br&gt;• Decrease malondialdehyde (MDA) hydrogen peroxide (H₂O₂)</td>
<td>30 g/day for 12 weeks</td>
<td>vivo</td>
<td>Human (sickle cell anemia patients)</td>
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<tr>
<td>Gum Arabic (Acacia Senegal) Augmented Total Antioxidant Capacity and Reduced C- Reactive Protein among Hemodialysis Patients in Phase II Trial (31)</td>
<td>• Gum Arabic significantly augmented total antioxidant capacity level&lt;br&gt;• Attenuated oxidative marker MDA&lt;br&gt;• Decrease C-reactive protein&lt;br&gt;• Increase hemoglobin level and RBC count</td>
<td>30 g/day for 12 weeks</td>
<td>vivo</td>
<td>Human (end-stage renal diseases (ESRD) patients)</td>
<td>27</td>
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<td>Gum Arabic Ameliorates Impaired Coagulation and Cardiotoxicity Induced by Water-Pipe Smoke Exposure in Mice (17).</td>
<td>• GA significantly mitigated thrombosis in pial microvessels in vivo, and platelet aggregation in vitro.&lt;br&gt;• Decrease Plasma concentrations of fibrinogen,&lt;br&gt;• Decrease plasminogen activator inhibitor-1&lt;br&gt;• Decrease lipid peroxidation,&lt;br&gt;• Decrease 8-isoprostane&lt;br&gt;• Decrease malondialdehyde.&lt;br&gt;• Increase glutathione, catalase and&lt;br&gt;• Increase Total nitric oxide levels in heart homogenates.&lt;br&gt;• Decrease nuclear factor erythroid-derived 2-like 2 (Nrf2) expressions by cardiac myocytes and&lt;br&gt;• endothelial cells,&lt;br&gt;• Decrease DNA damage and cleaved caspase 3,&lt;br&gt;• Decrease TNFα&lt;br&gt;• Decrease IL-1β</td>
<td>(15%, w/v) for 30 days</td>
<td>vitro &amp; vivo</td>
<td>Mice</td>
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<td>Gum Arabic Fibers Decreased Inflammatory Markers and Disease Severity Score among Rheumatoid Arthritis Patients, Phase II Trial (32)</td>
<td>• Decrease Serum TNFα, Decrease ESR, Decrease disease severity score DAS28</td>
<td>30g/dayGA for 12 weeks</td>
<td>vivo</td>
<td>Human (Rheumatoid Arthritis Patients)</td>
<td>28</td>
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<td>Gut Health-Promoting Benefits of a Dietary Supplement of Vitamins with Inulin and Acacia Fibers in Rats (33)</td>
<td>• Firmicutes, Actinobacteria phyla, Lactobacillus and Bifidobacterium spp) • Increase Calcium, Magnesium, Phosphorus, Zinc concentrations in the femur. GA has stronger prebiotic activity, which may lead to increasing mineral absorption.</td>
<td>4.5 g /100g (20% daily) for four weeks</td>
<td>vivo</td>
<td>Rats</td>
<td>29</td>
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<tr>
<td>Increment of Lysosomal Biogenesis by Combined Extracts of Gum Arabic, Parsley, and Corn Silk: A Reparative Mechanism in Mice Renal Cells (34)</td>
<td>• Combined extract • Increase GSH in serum • Decrease MDA in renal tissues • Decrease BAX expression • Decrease cytosolic expression of cathepsin D • Increase expression of nuclear TFEB (indicates active transcription of the lysosomal genes and autophagy), • Increase active expression of LAMP-1 • No signs of cellular degeneration in renal histology. (GA derived SCFAs act as mediators of intracellular GPR survival signals)</td>
<td>(3g/kg/day) for four weeks</td>
<td>vivo</td>
<td>Mice</td>
<td>30</td>
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<td>Role of L. plantarum KXS19413 as Probiotic and Acacia Gum as Prebiotic in Gastrointestinal Tract Strengthening (35)</td>
<td>• GA reinforced immunoglobulin levels and had a modulatory effect on phagocytosis, Decrease tumor necrosis factor α (TNF-α) levels, Decrease bacterial procarcinogenic fecal enzyme activities, Decrease triglycerides, Decrease LDL, Increase Calcium, Increase Phosphorous, Increase Ig A, (The consumption of a combination of the prebiotic and probiotic as a synbiotic was shown to exert many health-improving properties, such as Reduced blood lipid levels, regulation of immune function, and reduction of the levels of carcinogen-releasing enzymes. The maintenance of healthy gut microbiota by prebiotics and probiotics can be considered a striking route for retaining human and animal health statuses and disease prevention)</td>
<td>(1% in distilled water) for 3 weeks</td>
<td>vivo</td>
<td>Male Mice</td>
<td>31</td>
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<td>Title</td>
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| The Effect of Arabic Gum on Renal Function in Reversible Unilateral Ureteric Obstruction (36) | • Decrease Malondialdehyde  
• Decrease Superoxide dismutase  
• Decrease TNF-α  
• Decrease TGF-β1  
• Decrease p53 in AG-1  
• Attenuated the UUO-induced rise in oxidative stress markers and proinflammatory and profibrotic cytokines and the degree of renal tubular dilatation, indicating a protective effect in obstructive nephropathy. | 15 g/kg/day for 16 days | vivo        | Male Rats            | 32  |
| Waterpipe Smoke Exposure Triggers Lung Injury and Functional Decline in Mice: Protective Effect of Gum Arabic (18) | • Inhibited nuclear factor kappa-B (NF-κB) expression.  
• Augmented that of nuclear factor erythroid 2-related factor 2 (Nrf2).  
• Increase Cytoplasmic expression of glutathione in mice treated with GA and exposed to WPS.  
• Significant inhibition of the increase of TNF-α concentrations.  
• Augmentation of 8-isoprostane concentrations was significantly prevented by GA.  
• Abolished the increase of expression of NF-κB induced by WPS. | (15%, w/v) for 30 days | Mice       |                     | 15  |

**COVID-19 pathogenesis and the role of cytokine storm:**

Cytokine storm (CS) is an exaggerated complex immune response to external stimuli (3). CS is characterized by uncontrolled and excessive release of pro-inflammatory cytokines (5). Innate immunity is considered as the first line of defense against viral infection (33, 34). Hence, interferon (IFN-Ι or IFN-α/βis) represents the usual key immune defense reaction against viral infections and in the early stages of viral infection, IFN-I is the key player as an antiviral. The pro-inflammatory cytokine/chemokine response caused by rapid viral replication in lung epithelial and endothelial leads to the induction of apoptosis (35). The mechanism involves β and IFN γ through Fas–Fas ligand (FasL) or TRAIL–death receptor 5 (DR5) (36). In addition, unlike SARS patients, COVID-19 patients also presented with high levels of Th2 cell- secreted cytokines (such as IL-4 and IL-10), which delay the inflammatory response (3). The serum levels of IL-2 and IL-6 among COVID-19 patients are correlated with disease severity (37). The cytokine storm also plays a role in determining the prognosis of extra-pulmonary multiple-organ failure (38); explained by CS is the cause of damage to extra-pulmonary tissues and organs among some COVID-19 patients who did not develop respiratory failure (39).

Discrepancy in severe COVID-19, lymphocytes were activated as evidenced by high level of inflammatory cytokines, but patients have lymphocytopenia, (40). Rheumatologists believed that critical COVID-19 patients have shared the following: pathology with rheumatoid patients, unexpected deterioration within two weeks from infection, unexplained very low levels of lymphocytes, especially natural killer (NK) cells, as well as very high inflammatory markers, such as C reactive protein (CRP) and pro-inflammatory cytokines (IL-6, TNFα, IL-8) (5). In the same token, evidence of suppressed immunity among COVID-19 patients are
hypo-albuminemia, neutropenia and the diminished percentage of CD8+ T cells (4).

Alteration of the immune response could be explained through lymphocytes directly attacked by the virus or indirectly damaged by a Cytokine storm (CS) (5). COVID-19 infects target cells by angiotensin-converting enzyme 2 (ACE2), the latter is not expressed on lymphocytes. Therefore, it is probable that CS is the cause of lymphocyte destruction. (5). In addition to leukopenia, the other abnormal laboratory findings include altered function of the liver and an extremely increase in ferritin levels (41). The latter is unclear-- whether it be an epiphenomenon with diagnostic value or if the ferritin is involved in the vicious cycle of escalating inflammation (41). A postmortem lung examination of a COVID-19 patient with severe ARDS, revealed edematous, diffuse alveolar damage, desquamation, and hyaline membrane formation (4).

**Current modalities of treatment:** The quick dissemination of scientific knowledge nowadays, leading to several therapeutic interventions, which have been tested in small sample size studies. A few studies continued in larger sample size studies and other studies failed to continue into large and multi trials to show therapeutic benefits or impact on survival (42, 43). Currently, management of COVID-19 is not completed yet, but supportive treatment is necessary and respiratory failure, due to ARDS, is the main cause of death (44).

The use of a corticosteroid as anti-inflammatory medications may delay viral eradication and raise the risk of secondary infection, especially in immunocompromised patients (5). Scientists thought of immunomodulatory agents to reduce systemic inflammation before it results in organ dysfunction (5). There were further recommendations to add anti-cytokinic biological agents, such as anti-IL-1 (anakinra) or anti-IL-6 (tocilizumab (TCZ)) (45). These drugs were previously recommended for rheumatoid, autoimmune inflammatory diseases and have high efficacy and therapeutic benefits (41). Nevertheless, these biological agents inhibit only specific inflammatory and may not be efficient in downregulation of the CS in COVID-19 since other cytokines maybe of substantial importance (5) and the same concept is applied to NSAID (46). However, researchers and scientists are trying to generate strong evidence based on clinical trials to treat and manage COVID-19.

**Oxidative stress and COVID-19 pathogenesis:** Since inflammation is a key pathogenesis in COVID-19 patients (4), finding a way to block the CS utilizing anti-inflammation therapy is critical to reducing mortality (5). Immunocompromised patients and patients with metabolic syndrome, like type-2 diabetes, cardiovascular disorders are considered as high risk for mortality (47) -- and in such patients dysbiosis is involved and could cause an increase in the mortality rate (6).

Researchers assumed that oxidative stress is a part of COVID-19 pathogenesis (4). Viral infections inhibit NRF2-mediated pathways and NF-κB signaling activation, causing reduction of antioxidant defense and exaggeration of inflammation and oxidative stress (48).

**Modulation of gut microbiota as an immunomodulatory strategy against COVID-19 pathogenesis:** Gut microbiota involving short chain fatty acids (SCFA) like the butyrate, acetate and propionate have a protective role in health, through regulating a group of host physiological functions, secreting both immunomodulatory signals and metabolites signals (6, 49). Furthermore, it maintains an optimal immune system to attack the virus. Several studies proposed that modification of gut microbiota could lessen inflammation (50-52).
Nevertheless, the question of how this microbiota is linked to the lungs has yet to be answered. A previous study found that neonatal gut microbiota colonization can modulate lung immunity, which plays an important role in the “gut-lung axis” (53). This axis is bidirectional, which means lung inflammations can affect the gut microbiota causing a disturbance of activation and levels of leucocytes, lead to lung damage. The re-introduction of probiotics helps in recovery of the lungs through SCFA, or host derived products, such as cytokines and chemokines at lung and gut (54). Also, the re-introduction of probiotic strains, such as Bifidobacterium lactis into apparent healthy elderly volunteers resulted in a significant rise in leukocytes and the tumoricidal activity of NK cells (55-57).

COVID-19 influences the gut microbiota (58) and many studies have shown that alterations of gut microbiota is associated with inflammatory bowel diseases (IBD) (59), type 2 diabetes mellitus (60), depression (61, 62), cardiovascular disease (63) (64), hypertension (65), lung cancer in humans (66-68) and pneumonia (57, 69).

**Gum Arabic as prebiotic agent:** Prebiotics are defined as dietary elements that can modulate the gut flora, resulting in improving the host’s health and general wellbeing, with functional food effects (70, 71). In general, the term “Prebiotic” refers to food ingredients that are non-digestible and show beneficial effects on the host by stimulating the growth and/or activity of probiotics in the colon after fermentation” (72, 73). Gut microbiota metabolized polysaccharides and produce SCFAs, mainly butyrate, acetate and propionate (73).

Gum Arabic is a non-digestible dietary fiber and is mainly fermented by colonic intestinal bacteria (74-76). Dietary fibers are defined as carbohydrate polymers that are released after digestion and absorbed in the upper human intestine (77). Gum Arabic oral consumption increased the serum level of SCFAs, specifically Butyrate (19, 78, 79). Therefore, GA can be defined as prebiotic agent (80). Acacia exudates found to generate a significant increase in bifidobacteria and lactobacilli, compared to an equal dose of inulin; with less gastrointestinal complaints (29, 79, 80)

**Role of Gum Arabic as an immunomodulatory, anti-inflammatory, and antioxidant agent in COVID-19:** It has not yet been proven that Gum Arabic has a direct antiviral effect, although there are some Acacia species that exhibit antiviral activity against the hepatitis C virus (81). Nonetheless, GA exhibits an indirect effect through its anti-inflammation, anti-oxidation and immune-modulatory properties.

As mentioned above, viral load is not correlated with disease severity (82, 83), as the main pathogenesis is systemic inflammation and a cytokine storm (84), (82, 85) (40). Scientists suggested the addition of anti-inflammatory and stored to treatment regimens (5), (86).

In general, inflammation is associated with increased production of cytokines and chemokines, while GA causes an increase of anti-inflammatory cytokine IL10 (26) and a decrease in the pro-inflammatory cytokines, such as TNF-α, IL-1β, IL-6, and IL-8(22). GA significantly reduced TNF α among rheumatoid patients (28) and a shared pathogenesis between RA and COVID-19 has been established (5, 87).

Wapnir RA and his colleagues revealed that GA showed local anti-inflammatory effects by modifying nuclear factor-κB (NF-κB) on a small rat intestine (88). The anti-inflammatory effect of GA causes suppression of NF-κB activation not only in the small intestine in rats, but also in lung tissues in mice (15). The stimulation of NF-E2-related factor 2 (Nrf2) is important in protecting lungs from injury, though involvement of Nrf2 in COVID-19 is under study. However, areas with low prevalence of obesity (considering obesity a risk factor in COVID-19 severity) is associated with Nrf2 interacting nutrients intake; Hence, less severity of COVID-19, which attract
attention to the effect of Nrf2 as novel target therapy (89).

Gum Arabic has a strong antioxidant effect, which has been investigated in previous clinical trials among patients with sickle cell anemia. GA increased the TAC (total antioxidant capacity, associated with reduction in production of malondialdehyde (MDA), which enhances the antioxidant defense potentiality (25). This effect was detected by Ali NE et.al in hemodialysis patients when treated by 30g/day for 12 weeks (27).

Figure 1 summarized GA actions. Additional mechanisms that are of importance in COVID-19, GA through augmentation of Nrf2 expression in bronchial epithelial cells and alveolar cells which inhibits inflammation and oxidative stress (Figure 2).

In conclusion, the main pathogenesis of COVID-19 is due to inflammatory process and a cytokine storm. Thus, it is likely that GA consumption as prebiotic would be beneficial in supporting and controlling the inflammation and oxidation in coronavirus infected subjects as adjuvant therapy.

**Figure 1.** Potential pathway through which Gum Acacia (GA) influence gut-lung axis in COVID-19 pathogenesis.

Short-chain fatty acids (SCFAs) are the main metabolites produced after GA fermentation in the large intestine. GA might influence gut-lung axis and lung function directly or indirectly. Indirectly through the health benefits of SCFAs and directly through the direct effect of GA on balancing the proinflammatory cytokines and the anti-inflammatory cytokines, hence reduce the cytokine storm (CS) in COVID-19. GA as strong prebiotic produces mainly butyrate. Through binding to G protein-coupled receptors (GPCRs) GA reduces the pro-inflammatory cytokines; tumor necrosis factor (TNF-α), interleukin-6 (IL-6), interleukin-8 (IL-8), and C-reactive protein (CRP), by which are considered as important cytokine storm (CS) markers in COVID-19. On the other hand, GA induces production of anti-inflammatory cytokines; interleukin-10 (IL-10) and interleukin-4 (IL-4). GA reduces the oxidative reactive stress (ORS) markers. GA influences intestinal mucosal immunity, and barrier integrity and function, systemically by leading to activation, and regulation of whole-body energy homeostasis. Peripherally GA systemically balances inflammation mainly by regulating the secretion of interleukins in COVID-19 disease.
COVID-19 and Gum Arabic in high-risk groups: Metabolic diseases are a worldwide public health issue associated with high morbidity and mortality (90). Obesity is considered the risk factor for impaired metabolic function, T2D, dyslipidemia, hypertension, and cardiovascular disease (91)

Obesity is associated with dietary fiber intake and explained by increased systemic low grade inflammatory markers, due to excess adipose tissue. The imbalance between anti-and pro-inflammatory cytokines results in abnormal chemotaxis and macrophage differentiation, which compromises immune function (92). The innate response associated with obesity causing high release of pro-inflammatory elements correlates with COVID-19 severity (93). Several experimental studies confirmed the association between dietary fiber intake and obesity, body weight, cholesterol and blood glucose.

Gum Arabic decreased food intake and body weight, which were associated with the reduction of abdominal visceral adipose tissue (VAT). This effect occurred either by altering the satiety (94-96), gastric emptying (97) or altering glycaemic index (97-98).

In clinical trials, GA was consumed by diabetic patients for 12 weeks, which resulted in a significant reduction of fasting blood glucose levels and glycosylated hemoglobin (HbAc1) (99). This might be explained a study in which experimental mice GA inhibits absorption of glucose in the intestine by their action on membrane abundance of sodium-glucose transporter 1 (SGLT1) (100,101). Thus, GA may prevent and/or manage obesity, while reducing the impact of COVID-19 in high-risk patients.

Figure 2. Potential pathway through which Gum Acacia (GA) influences COVID-19 pathogenesis.

GA and butyrate inhibited the induced downregulation of Nrf2

GA directly augments nuclear factor erythroid 2-related factor 2 (Nrf2) and increases the nuclear expression of Nrf2 of bronchial epithelial cells and alveolar cells. GA increase production of butyrate hence it inhibits the down-regulation of Nrf2 caused by SARS-CoV-2. SARS-CoV-2 infection down-regulates the expression of angiotensin converting enzyme 2 (ACE2) and increase angiotensin II (Ang II), thus leading to increased vasoconstriction, inflammation, fibrosis, lung damage and oedema. On the other hand, ACE2 inactivates (Ang I). Ang I interact with G protein coupled receptor (GPCR) Mas to produce a vasoprotective action to the lung; this mechanism is inhibited by over-activation of Ang II by SARS-CoV-2 infection. GA reduces oxidative stress markers and increase nitric oxide (NO) to imbalance the ORS/NO ratio and prevent inhibition of the vasoprotective action through effect of butyrate and direct augmentation of Nrf2 expression in bronchial epithelial cells and alveolar cells.
CONCLUSION: Gum Arabic is a potent prebiotic with potential effect to reduce the cytokine storm by balancing the pro-inflammatory and anti-inflammatory response in humans. The potential effect of GA as an antioxidant, anti-inflammatory and immunomodulatory of lung-gut axis balancing activity plays an important role in the adjuvant treatment of COVID-19 infections in human. There should be an increase in GA research to further clarify the actual physiological mechanism at a molecular level. This review may create an innovation in dietary interventions to boost immunity and counteract COVID-19 disease.


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