SHORT FEATURE

Resistant Starch
Could This Immunity Booster Play a Positive Role in COVID-19 Management?

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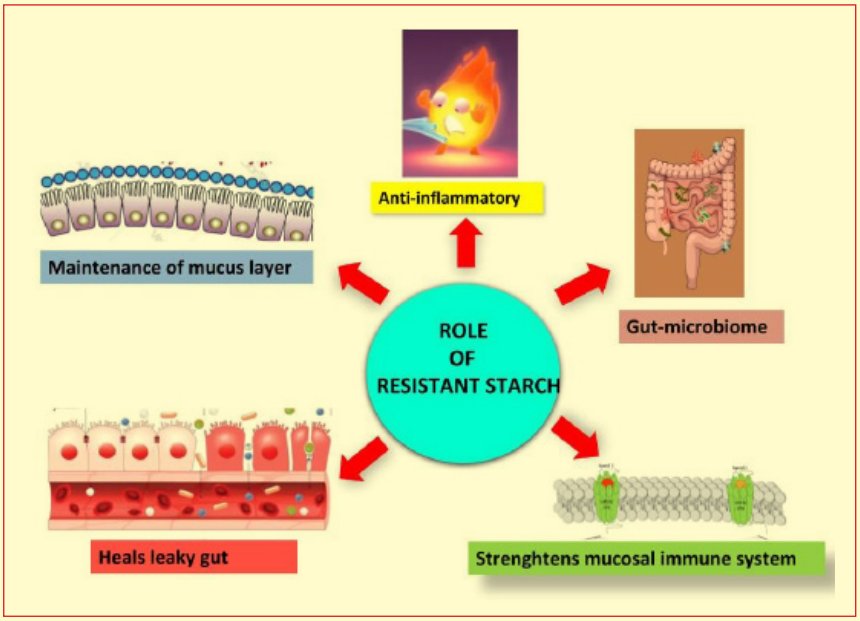
A tiny virus of 0.125 microns diametre has created mayhem globally and has potentially changed even the time zone to pre- and post-coronavirus disease (COVID) era. Even though global attention is focused on developing vaccines, various preventive suggestions highlight the power of immunity as a potential weapon against this pandemic.

Medical practitioners suggest the need for a proper diet plan including vitamins and bio-actives, which are functional moieties that balance both arms (cellular and humoral immune response) of immunity. Mounting evidence and reports on the role of phytochemicals and whole grains as immunity boosters thus justify the most prominent link between diet and immunity.

Researchers are now trailing different kinds of immunity boosters like Resistant Starch (RS), honey, vitamins, zinc, and omega-3 to check their activity against COVID infections. Recently, the ICAR-Indian Institute of Millet Research (IIMR) has reported that millets, a richer source of resistant starch, could be an efficient diet component to tackle COVID-19. However, better understanding of how they provide immunity compared to staple cereals like rice and wheat is still required.



Functional role of resistant starch

Immunity and Resistant Starch

The immune system (innate and adaptive immune response) is a means of protection against the damaging effects of noxious pathogens, which cause infection in our bodies. So, adequate and appropriate nutrition is required for all cells to function optimally and this includes the cells in the immune system as warriors.

A positive correlation has been observed between diet and immunity in various lifestyle disorders, chronic inflammatory diseases such as intestinal bowel disease, colorectal cancer, allergies, autoimmune diseases, and obesity and its associated pathologies. Researchers have been giving emphasis on the beneficial role of dietary fibre which modulates the biological roles of the gut microbiome and ultimately maturation of the immune system. There could thus be a possible role for resistant starch in managing COVID-19 as well.

***Resistant starch as anti-inflammatory molecules*:** In COVID cases, we have seen prevalence of lung associated inflammation which ultimately increases the inflammatory biomarkers like C-Reactive Proteins, cytokines

like Interleukins (IL-6), and Tumour Necrosis Factor (TNF-α.). In a systematic review and meta-analysis, Vahdat *et al.* (2020) have reported that the consumption of resistant starch significantly reduces the levels of such inflammatory biomarkers. Recently a study has come out from UK's Anglia Ruskin University (ARU) in collaboration with Queen Elizabeth Hospital King's Lynn NHS Foundation Trust, which mainly focused on the role of resistant starch and Vitamin D in modulating the response of white blood cells and found their role in releasing anti-inflammatory cytokines, thereby preventing inflammatory conditions like COVID infection.

Impact of resistant starch on gut-microbiome: Resistant starch nourishes the gut microbiome with lactate, acetate, propionate, and butyrate. Butyrate creates an acidic environment to proliferate colonic and cecal cells, increase the expression of gut genes and decrease ileal and cecal digesta pH, which in turn promote the growth of beneficial microorganisms (Haenen *et. al.*, 2013). Acetate provides energy for the metabolism of distal organs like spleen, heart and brain. Propionate can inhibit the synthesis of cholesterol and fatty acids in the liver, thereby decreasing blood lipid levels and butyrate usually reduces the pH in the colon and thus inhibits the proliferation and metastasis of pathogenic bacteria. (Heo *et al.,* 2014). Studies have shown that incorporation of various types of resistant starch in diet benefits gut health by impacting the relative abundance of microbial species as well as through their metabolites.

Resistant starch maintains gut mucosal layer: The gastrointestinal epithelium is covered by a thick mucus gel which performs various functions like lubricant, protective barrier against microbes and preventing noxious substances from reaching the surface of the epithelium. The outer layer of the mucus is populated by many types of bacteria while the dense, inner layer is largely bacteria-free in healthy individuals. This dense inner layer also contains anti-microbial peptides and secretory antibodies that help protect the epithelial layer from pathogens (Camilleri, M. 2019). If the intestinal bacteria are under-fed, they will consume the mucus as food. Dr Eric Martens and his colleagues demonstrated that fibre-free diets erode the mucus barrier (Desai *et al.*, 2016). Dr Michael Conlon and his CSIRO colleagues have shown that dietary resistant starch from corn has a role in protecting the mucus layer and prevented the damage caused by the high protein diets (Toden *et al.,* 2007).

Resistant starch heals leaky gut: An unhealthy gut lining may have large cracks or holes, allowing partially digested food, toxins, antigens and bacteria in the lumen to enter the bloodstream creating a "leaky gut". This may trigger inflammation and changes in the gut flora (normal bacteria) that could lead to problems within the digestive tract and beyond. An animal study by Dr Martin Kriegel and his colleagues at Yale University (Zegarra-Ruiz *et al.,* 2019) demonstrated that resistant starch from corn helped to heal the leaky gut. In line with that, Nofrarias *et al.,* (2007) reported that resistant potato starch improved the colonic mucosal integrity of pigs and Qin *et al.,* (2019) said resistant potato starch improved gut barrier integrity of meat ducks.

Resistant starch strengthens mucosal immune system: Innate mucosal immunity plays a significant role in pathogen trafficking in the body. It recognises pathogens using its various molecules and triggers cascades of signals to eliminate the foreign body, induce tissue repair, and further trigger the adaptive immune response. Camilleri, M. (2019) reported that butyrate, a product of fermentation of resistant starch, interacts directly with the immune system through surface transmembrane G Protein-coupled Receptors (GPCRs) and inhibits histone deacetylase and directly alters the expression of intestinal genes (Chang *et al.,* 2014) and induced antimicrobial activity in intestinal macrophages (Schulthess *et al.,* 2019).

Resistant starch and the gut lung axis: Even though COVID-19 is a respiratory illness, the gut too has an invisible role. Changes in one compartment could impact the other compartment, whether in relation to microbial composition or metabolite mediated action. Several studies have shown that gut immunity could be transmitted to distal organs through the transit of microbes or through metabolites like SCFA. SCFAs, mainly produced by the bacterial dietary fermentation especially in case of a high-resistant starch diet, have known directly to play a role in the gut by production of beneficial microbes and also acting in the lungs as signalling molecules on resident antigen-presenting cells to attenuate the inflammatory and allergic responses (Anand and Mande., 2018; Cait *et al.*, 2018). Therefore, diet, prebiotics, or more specific modulations could become novel essential tools in therapeutic management of COVID-19, especially including high resistant starch in daily diet.

Even though the Recommended Dietary Allowance (RDA) of dietary fibres like resistant starch is 38g/day (Adult men) and 25g/day (Adult women), higher intake could be recommended in this testing time. Unripe banana, whole grain cereals, pigmented rice, jackfruit seeds and legumes are rich sources of resistant starch.

A clinical study has already been initiated by Yale University in collaboration with the University of Michigan and the University of Minnesota to evaluate the efficacy of resistant potato starch in reducing rates of hospitalisation and improving time of clinical recovery in non-hospitalised COVID-19 patients. The role of resistant starch isolated from various sources like pigmented rice in COVID-19 patients needs to be further scientifically validated.

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