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# Probiotic Proceedings of Lactobacillus and Bifidobacterium on Individual Vigor Remuneration: Contemporary Standing

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**ABSTRACT**
*During the phase of COVID 19, people of whole world were facing the biggest challenges of health problems. Everyone looking for the better options to enhance the immunity of the body to protect themselves from various viral and bacterial infections. Several nutritional supplements and functional foods are available which enhance the immunity of the body simultaneously fulfil the nutritional requirements. But these are insufficient to make body fit and ready to fight against outer enemies, microbial infections and several health problems. Probiotic is established to fill this gap as it has group of live beneficial microbes which provides health benefits to the hosts and protect them from microbial infections and various health problems. One of the most significant aspects of probiotics is that they have proven to be safe, cheap and capable of hindering with microbial infection. Probiotic also play a pivotal role in keeping up the resistance and the metabolic homeostasis effective to protect against pathogenic microbes. Use of probiotics is rapidly expanding with the globalization of functional food and health supplements. Various probiotic products are available containing different specific probiotic strains for specific health problems. Beneficial role of Probiotic microbes is strain specific and all the probiotic strains are lies under the genera of Lactobacillus, Bifidobacterium, Bacillus, Streptococcus, Enterococcus, Lactococcus, Leuconostoc, Saccharomyces. But most of the probiotic strains lies under the genera of Lactobacilli and Bifidobacterium. Therefore, the present review focuses on the beneficial role of potential strains of Lactobacillus and* Bifidobacterium *in various health problems.*
***Key words***: *Probiotics, Synbiotic, Lactobacillus, Bifidobacterium, Lactic acid bacteria, Human health*

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## INTRODUCTION

In 1953, the German Scientist Werner Kollath was introduced the term probiotics by which to mean "active substances essential for a healthy life" [1]. FAO/WHO in 2002 given the world wide accepted definition of probiotic that live microorganism which when administered in adequate amount confer health benefits to the host. All probiotic strains come under the category of Lactic acid bacillus as all are have characteristic to produce lactic acid by the fermentation of carbohydrate sugar. Based on certain health promoting properties such as resistance to enteric pathogens, aid in lactose digestion, modulation of immune system and decreasing detoxification/excretion of toxic microbial metabolites [2], probiotics have emerged as the chief nutritional factor and laid down new opportunities for the food and nutrition field for scientists to improve food quality and develop new products with specific health benefits for different sub populations [3]. More specifically probiotics are active microorganism which benefit the host by improving the health of gastrointestinal tract through establishment of healthy microflora [4]

Probiotics have been investigated to determine potential beneficial effects in the prevention and treatment of a wide variety of systemic conditions. These conditions include rebalancing the population of bacteria in the gut, aiding digestion, inflammatory and autoimmune diseases such as rheumatoid arthritis, ulcerative colitis, multiple sclerosis, and hepatic encephalopathy [5]. Probiotics are considered as boon to improve the Gut health by colonizing healthy bacteria capable of producing various vitamins and essential metabolites for normal growth and development.

The most important characteristic of probiotic strains is that they generally considered to be safe for human consumption. Therefore, WHO considered maximum probiotic strains as GRAS (generally recognized as safe). However, various regulatory bodies from different countries specify some important parameters or characteristics for the potential strains which need to be tested before its commercialization or consumption. To be used as a probiotic, the selected strain must be able to tolerate gastrointestinal conditions, mucosal adhesions, and deprivation of competition [6]. Additionally, they should possess the abilities such as pathogen exclusion, anti-oxidant, antimicrobial, immuno-modulatory and food fermentation. Probiotics are also reported to be useful in modulating Human health [7, 8]. Most commonly micro-organisms used as probiotics belong to the heterogeneous group of lactic acid bacteria (genera Lactobacillus and Enterococcus) and the genus Bifidobacterium. Each group involves different species (*Lactobacillus acidophilus*, *Bifidobacterium bifidum*, etc.), including different strains [9].

Potential strains of Lactobacillus and Bifidobacterium, have been widely used as effective probiotics [10]. Lactobacillus and Bifidobacterium have been suggested to be associated with alleviation of lactose intolerance; prevention and cure of diarrhoea caused by viral, bacterial, and antibiotic or radiotherapy, immunomodulation; antimutagenic and anticarcinogenic effects and physiological and metabolic changes like reduce the body fat 14, blood cholesterol [11, 12].

There are many sources of exposure to Lactobacilli and Bifidobacteria. These sources include probiotics, fermented foodstuffs (e.g., yogurt, cheese, sauerkraut, Sourdough bread, Pickles, Beer, wine, cider and many other fermented foods), as well as the host's own microflora. In many traditional foods, such bacteria play an important role in preventing spoilage and the growth of pathogenic microorganisms. Some probiotic products that contain lactobacilli or *bifidobacteria* have long histories of safe use in some cases, for many decades [13]. They inhibit the growth of other harmful bacteria with lowering the pH by producing lactic acid and preserve the nutritive qualities of raw food material for an extended shelf life [14-16]. In healthy humans, lactobacilli are normally present in the oral cavity (103 –104cfu/g), the ileum (103 –107cfu/ g), and the colon (104 –108cfu/g), and they are the dominant microorganism in the vagina. Increasing consumption of probiotic lactobacilli and *bifidobacteria* has not led to opportunistic infections in consumer [18]. However, infection due to lactobacilli and *bifidobacteria* are extremely rare and are estimated to represent 0.05%–0.4% of cases of infective endocarditis and bacteremia [17]. Lactobacilli constitute an integral part of the healthy gastrointestinal (GI) microecology and are involved in the host metabolism [19].

Due to fast growing awareness about the benefits of probiotic among the consumers, people looking for different probiotic products and health supplements to get health benefits and to boost their immunity to fight against different health problems. Therefore, various synbiotic (Probiotic and Prebiotic) products containing different strains of Bifidobacterium and Lactobacilli are introduced in the market by the probiotic manufactures for different health application. Furthermore, the growth and market size of probiotic products also increases day by day. Probiotics have widely been used in food, dairy, Pharmaceuticals, Nutraceuticals and fermentation as well as non-pharmacological sectors [20].

**General Characteristic:**

The most commonly used strains of Lactobacilli spp are *Lactobacillus acidophilus, Lacticaseibacillus rhamnosus, Lacticaseibacillus casei, Lacticaseibacillus paracasei, Lactiplentibacillus plantarum, Limosilactobacillus fermentum, Limosilactobacillus reuteri, Levilactobacillus breve, Lactobacillus gasseri, Lactobacillus helveticus, Lactobacillus johnsonii* and many more. Similarly, the most common strains of Bifidobacterium spp. are *Bifidobacterium bifidum, Bifidobacterium longum, Bifidobacterium brevis, Bifidobacterium animalis, Bifidobacterium infantis* etc.

Lactobacillus are rod shaped, gram positive, catalase negative, non- motile, oxidase negative, endospore forming, fermentative, facultative anaerobic or microaerophilic bacteria [21-23]. In most cases they form chains of varying length. Lactobacilli have a generation time from 25 to several hundred minutes. In humans and animals, they are found in the intestinal track and perform many beneficial functions including immunomodulation, suppression of enteric pathogens and maintenance of intestinal flora. Species of *Lactobacilli* are mostly homofermentative, but some are heterofermentative. The genus has been divided into three major subgroups and over 70 species are recognized [24].

*Bifidobacterium* are gram-positive, non-spore forming, anaerobic, pleomorphic bacteria [25-28]. *Bifidobacteria* have been shown to represent one of the most abundant genera present in a healthy gut early in life, being the most abundant genus present in the intestine of healthy breastfed infants, and to play an important role in gut homeostasis and immune system development [29-32].

**Some Common health benefits of strains of Lactobacilli and Bifidobacterium spp. are:**

- They can help to improve the health problems related to heart.
- They can also help to provide relieve in the problem of lactose intolerance.

- They are helpful in various food and skin allergies.
- They can reduce inflammation in the vagina due to an overgrowth of bacteria.
- They can improve unpleasant odor in exhaled breath.
- They help to reduce the frequency and duration of diarrhea.

**Some best probiotic strains of Lactobacilli and Bifidobacterium for health benefits include:**

- ***Lactobacillus plantarum*** (*Lactiplantibacillus plantarum*) inhibits the growth of harmful bacteria. They stimulate the digestive system, fights off disease-causing bacteria, and helps the body to produce vitamins.
- ***Lactobacillus acidophilus*** regulates stomach acidity levels.
- ***Lactobacillus paracasei (Lacticaseibacillus paracasei)*** strengthens the immune system.
- ***Lactobacillus fermentum (Limosilactobacillus fermentum*)** strengthens immune system and prevents gastrointestinal and upper respiratory infections
- ***Lactobacillus reuteri (Limosilactobacillus reuteri)*** supports heart health by balancing cholesterol levels. It also reduces ulcer-causing bacteria and supports female urinary tract and vaginal health.
- ***Lactobacillus delbrueckii*** subsp.*bulgaricus* is supports good digestion, prevents diarrhoea, and helps relieve symptoms of irritable bowel syndrome (IBS).
- ***Lactobacillus rhamnosus (Lacticaseibacillus rhamnosus*) *is*** naturally found in your gut, although you can eat foods or take supplements to increase its benefits. It's helpful in relieving IBS symptoms, treating diarrhoea, strengthening your gut health, and protecting against cavities.
- ***Bifidobacterium longum ssp. Infantis*** is commonly used to treat bowel problems, eczema, vaginal yeast infections, lactose intolerance, and urinary tract infections.
- ***Bifidobacterium bifidum*** can help manage your digestive system, improve IBS, and boost your immune system.
- ***Bifidobacterium animalis ssp. Lactis*** helps prevent infection. It helps to break down carbohydrates and synthesize vitamins.

  Different beneficial roles of some important strains of Bifidobacterium and Lactobacilli are included in **Table 1.**

**Table 1: Some best strains of Lactobacilli and Bifidobacterium which modulate the human health**

| | **Probiotic effect on** Culture/ combination used | **Dosage and duration** | **Function** | **Reference** |
|---|---|---|---|---|
| **1** | **As neuroprotectants** | | | |
| | *L. acidophilus*, *L. casei*, *B. bifidum*and *L. fermentum* | 2 X $10^9$ CFU/g each for 12 weeks. | Improved cognitive function and suppress inflammation | [31] |
| **2** | **Combating stress and depression** | | | |
| | *L.acidophilus, L. rhamnosus, L. paracasi, L.plantarum, L.returi, B. longum, B.lactis* | 50 billion for 28 days | Reduce detrimental effects of stress on cognition | [32] |
| **3** | **Skin problems** | | | |
| | *B.lactsB.longum*and *L.casei* | 1 X $10^9$ CFU/g each for 12 weeks. | Effective in reducing SCORAD index and reducing the use of topical steroids in patients with moderate AD. | [33] |
| **4** | **Rheumatoid arthritis** | | | |
| | ***L. acidophilus, L. casei, Bifidobacterium bifidum*** | 2 × $10^9$ CFU, for 8 weeks. | Improved Disease Activity Score of 28 joints , insulin levels, and hs-CRP levels | [34] |
| **5** | **Anticancer agents** | | | |
| | ***L.plantarum L.acidophilus and B.longum*** | $10^{11}$ CFU, for 16 days | Probiotics decreased the serum zo nulin concentration, duration of postoperative pyrexia, inhibite the p38 MAP kinase signaling pathway. | [35] |
| **6** | **Metabolic abnormality** | | | |
| | Probiotic capsule: *L. acidophilus, B bifidum, L. casei, L. fementum* | $10^{10}$ CFU, 12 week | Reduce the lipid levels and hs-CRP levels | [36] |

| | | | | |
|---|---|---|---|---|
| | *L. acidophilus,*<br>*L. casei,*<br>*L. rhamnosus,*<br>*L. bulgaricus,*<br>*Bifidobacterium breve,*<br>*B. longum,* | $2X10^{11}$ CFU, 6 week | Reduce the Blood glucose and HbA1c levels | [37] |
| **7** | **Allergies** | | | |
| | *L. rhamnosus* | $2×10^{10}$ CFU,for 6 months | Effective in inducing possible sustained unresponsiveness and modulation of the immune response. | [38] |
| **8** | **Respiratory tract infections** | | | |
| | *L. rhamnosus* | $2 X 10^9$CFU, For 60 day | Reduce the No. of days in episodes with fever, diarrhea, and respiratory Illness | [39] |
| | *L.rhamnosus*<br>*B.breve P.shermanii* | $2 X 10^9$CFU for 6 month | | [40] |

**Health benefits and superiority of Lactobacilli and Bifidobacterium strains over other Strains of Lactic Acid Bacteria:**

The digestive system as well as mucous membranes constitute natural sites of Bifidobacterium, whereas Lactobacillus bacteria inhibit the digestive and urogenital systems. *Bifidobacteria* are among the first colonisers of the sterile gastrointestinal tract of new born during breast feeding. Most strains of Lactobacilli can ferment amygdalin, cellobiose, fructose, galactose, glucose, lactose, maltose, mannose, salicin, sucrose and trehalose [41-45]. The genus of Bifidobacterium may, with the assistance of intracellular enzymes, break down polysaccharides which undergo conversion into glucose and fructose phosphates.

It was reported that Lactobacillus and Bifidobacillus containing probiotics were found to improve outcomes in acute infectious diseases outside of the gastrointestinal tract, such as upper and lower respiratory tract illnesses in infants and college students [46, 47]. It was also reported that the addition of fermenting *Lacticaseibacillus paracasei* to milk or rice milk resulted in reduced episodes of gastroenteritis, rhinitis, otitis, laryngitis, and tracheitis [48]. These finding suggested that the benefits to the host extend beyond local interactions in the intestinal tract between the gut organisms, enterocytes, and the immune system, perhaps involving microbial metabolites and/or migrating dendritic cells that reach distant locations such as the spleen and lymph nodes.

Lactobacilli and Bifidobacterium spp have been found to control intestinal disorders through a number of mechanisms to prevent destructive or pathogenic bacteria from mounting on and attaching to the intestinal epithelium: viz production and secretion of antimicrobial agents such as bacteriocins and organic acids [49, 50]. Bacteriocins are small proteins that have properties such as antitumour and anticholesterol activity which constitute a heterologous sub group of ribosomally synthesized antimicrobial peptides [51-53]. Bacteriocins have been reported to permeate the outer membrane and to induce the inactivation of Gram-negative bacteria in conjunction with other enhancing antimicrobial environmental factors, such as low temperature, organic acid and detergents [54, 55]. Some studies are also demonstrated that by products produced by *Lactobacillus spp* inhibited the growth of fungi such as *Aspergillus niger, Cladosporium herbarum and Penicillium verrucosum* in food materials [56, 57].

*Bifidobacterium longum* is the most frequently reported Bifidobacterium spp. having health benefits include competing with harmful bacteria for nutrients, colonization numbers and adherence to the intestinal epithelium. Control of epithelial cell proliferation and differentiation and homeostatic regulation of the immune system are tropic functions [58-60]. *Bifidobacteria* expand the number of mucosal lymphocytes, the size of germinal canters in lymphoid follicles and there is some research indicating a role in the induction of regulatory T cells in lymph follicles [61].

**Mechanism of Action:**

Mechanism of probiotic can be described as stimulation of phagocytic activity, complement-mediated bacterial killing, and immunoglobulin production [62, 63].

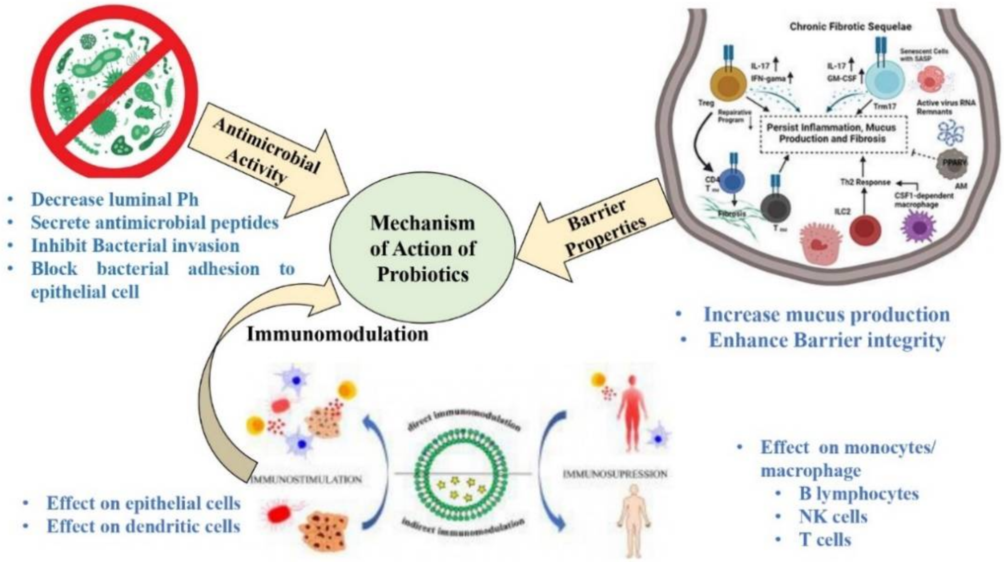


**Figure 1: Mechanism of action of probiotics**

**Paraprobiotics and Postbiotics properties of Lactobacilli:**

Parabiotics can be well described administration of small amount of inactivated microbial cells or cell fractions which can deliver health benefit to host [59]. On the other hand, the soluble products generated as a result of metabolism of probiotics are termed as postbiotics. These products have also been reported to confer health benefits to host [64].

Both paraprobiotics and postbiotics can efficiently be extracted from specific probiotic bacteria using techniques such as, thermal treatment, enzymatic treatments, solvent extraction, radiation (ionizing and UV rays) and many more [60, 61, 34] Postbiotics consist of secreted proteins and peptides, bacteriocins, organic acids [65]. Both endure health promoting properties such as immunomodulatory, anti-tumor, barrier-preservation, and antimicrobial properties [66]. Paraprobiotics comprises of peptidoglycans, surface proteins, cell wall polysaccharides. These properties of Lactobacilli are included in **Table No.2**.

**Table 2: Paraprobiotic of some Lactobacilli strains and health benefits:**

| Probiotic | Active component | Specificity | Beneficial effect | | References |
|---|---|---|---|---|---|
| | | | **Strain** | **Effect** | |
| *Lactobacilli* | Peptidoglycan | Polymer of repeating units of N-acetylglucosamine and N-acetylmuramic disaccharide | *Lactobacillus casei, Lactobacillus johnsonii, Lactobacillus plantarum* | Suppress interleukin-12 (IL-12) production, preventing inflammatory bowel diseases | [66-69] |
| | | | *Lactobacillus salivarius* | Anti-inflammatory properties | |
| | | | *Lactobacillus rhamnosus* | Boast Innate and systemic adaptive immune responses in mice | |
| | Teichoic Acid | Covalently linked to peptidoglycan | *L. plantarum* LTA | Anti-inflammatory effects and immunomodulatory properties | [70] |
| | Cell-Wall Polysaccharides | Exopolysaccharides providing the interaction of the bacteria with the environment | *L. rhamnosus* | Immuno-suppressive effect | [71, 72] |
| | | | *L. plantarum* | anti-inflammatory effect, response against enterotoxigenic, | |
| | | | *Lactobacillus delbrueckii* | Anti-viral property | |

| | | | | | |
|---|---|---|---|---|---|
| | | | *Lactobacillus acidophilus* | Effective against colon cancer | |
| | **Cell Surface Proteins** | Attached to cell surface via covalent or non-covalent linkage | | | |
| | LPXTG Proteins | Comprising of LPXTG signal and forms linkage with cell wall via sortase A (SrtA) | *L. plantarum* and related species | Initiate bacteria-host interaction | [73-75] |
| | S-Layer Proteins | Linked to peptidoglycan via non-covalent linkage | *Lactobacillus paracasei subp. paracasei, L. rhamnosus, L. casei* | Prevent the infection of pathogenic bacteria<br>Prevent the adherence of *Shigella sonnei* | [76] |
| | | | *L. helveticus* fb213, *L. acidophilus* fb116 and *L.* | facilitate the adhesion of *Lactobacillus* and inhibit *E. coli* ATCC 43893 adhesions | |
| | Moonlighting Proteins | assist the colonization of probiotic strains in intestinal tract | *L. plantarum*, *Lactobacillus fermentum* (*L. fermentum*), and *L.* | Prevention of pathogens in intestinal tract | [77] |

**Probiotic products containing potential strains of Lactobacilli and Bifidobacterium spp.:**
Lactobacilli are often found in dairy products and other probiotic functional food. *Lactobacillus delbrueckii* subsp *bulgaricus* are used in the preparation of yogurt; *Lactobacillus acidophilus* is used in the preparation of acidophilus milk; *Lactobacillus helveticus*, as well as *L. delbrueckii* subsp *bulgaricus*, are used to make Swiss, Mozzarella, provolone, Romano, and parmesan cheeses etc. The lactobacilli are usually more resistant to acidic conditions than are other LAB, being able to grow at pH values as low as 4. This enables them to continue to grow during natural lactic fermentations when the pH has dropped too low for other LAB to grow, so they are often responsible for the final stages of many lactic acid fermentations. Bifidobacterium spp is an extremely versatile strain found in foods such as yogurt and fermented milk [78]. Apart from above, several species of probiotic are also used in the preparation of various Pharmaceuticals and Nutraceuticals probiotic and Synbiotic products which are available in the markets as a single culture or combination of multi strains in different forms like capsules, Sachets, dry syrup, tablets, gummies etc. [79, 80]. Synbiotic contains the benefits of both probiotics and prebiotics. Prebiotics are generally inactive ingredients and dietary fibres which are not easily digest by the body and it act as food for probiotic strains and helps them to grow. There are various prebiotics ingredients like Fructooligosaccharide, inulin etc. which are commonly used by the manufacture in the preparation of synbiotic products. Some common probiotic functional foods and probiotic strains are included in **Table no. 3.**

**Table 3: Some Probiotic functional foods containing potential strains of Lactobacilli and Bifidobacterium:**

| **Product** | **Probiotic Strain** | **Health benefits** | **References** |
|---|---|---|---|
| Kefir | *Lactobacillus spp.* | Anti-Hypertensive, Anti-Cancer, Anti-inflammatory | [81-83, 89] |
| Sauerkraut | *Lactobacillus plantarum, Lactobacillus brevis,* | Anti-inflammatory, Anti-Cancer, Treats skin infections, Reduces oxidative stress | [84] |
| Kimchi | *Lactobacillus plantarum,* and *Lactobacillus brevis* | anticancer, antiobesity, andanti-atherosclerotic | [85, 86] |
| Pickles | *Lactobacillus plantarum,* and *Lactobacillus pentosus* | Antimutagenic, cholesterol-lowering effects | [85] |
| Yoghurt | *Lactobacillus plantarum 201 LRR* | Improves digestion, Anticarcinogenic, anti-diabetic, Hypocholesterolemic effect, anti- diarrhoeal | [86, 87] |
| Yakult | *Lactobacillus spp.* and *Bifidobacterium spp* | | [88] |

### Major players in the field of probiotics Market:

The probiotic market of is assigned into three categories based on product viz. probiotic food & beverages, probiotic dietary supplements, and animal feed probiotics. The major key players operating in this market comprises of BioGaia A.B, Danone, Chr. Hansen Holding A/S, Yakult Honsha Co. Ltd., Probi A B, Lifeway Foods, Inc., Nestle S.A., Ganeden, Inc., E. I. du Pont de Nemours and Company, and Protexin. Brands that exist in Indian probiotic industry are Nestle, Amul, Yakult Danone and Mother Dairy along with other minor players operating in different regions in their own capacities.

## CONCLUSION

Most of the potential strains of probiotic lies under the genera of Lactobacilli and Bifidobacterium. It is well established that probiotics have impact on the immune system and this interaction is directly linked to gut microbes, their polysaccharide antigens, and key metabolites produced by probiotic strains. Gut microbiota modification with specific probiotic and Synbiotic products containing potential strains of Lactobacilli and Bifidobacterium spp. might offer a novel and cost-effective therapy to reduce the risk of number of diseases. Probiotic functional foods as well us dietary supplements containing potential strains of Bifidobacterium and Lactobacillii are capable to boost immunity as well as provides health benefits in several health problems. However, awareness needs to be created in general public for the selection and consumption of correct probiotic products to get health benefits. Also, future research needs in terms of the underlying mechanism of action involved in each of the observed effects. Advanced techniques such as encapsulation of probiotic bacteria can be undertaken to produce food products with beneficial effect.

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## CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

## AUTHOR CONTRIBUTIONS

Mithilesh Jaiswal: Writing – original draft, Visualization, Editing
Kajol Batta- Writing – original draft, Editing and Revising
Juhi Sharma: Visualization, Editing
Shyamji Shukla: Supervision
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