(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
03 October 2024 (03.10.2024)

WIPO | PCT

(10) International Publication Number
WO 2024/201522 A1

(51) International Patent Classification:
A61K 31/00 (2006.01) *A61K 31/716* (2006.01)
A61K 31/702 (2006.01) *A61K 33/00* (2006.01)

(21) International Application Number:
PCT/IN2024/050327

(22) International Filing Date:
27 March 2024 (27.03.2024)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
202341021937 27 March 2023 (27.03.2023) IN

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(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CV, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IQ, IR, IS, IT, JM, JO, JP, KE, KG, KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, MG, MK, MN, MU, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, WS, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, CV, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SC, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, ME, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Published:
— *with international search report (Art. 21(3))*
— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))*

WO 2024/201522 A1

(54) Title: NUTRACEUTICAL COMPOSITION FOR ORAL ADMINISTRATION

(57) Abstract: The present application relates to a oral composition comprising nutrients to address the nutrition deficiency in human subjects. Particularly the application relates to oral compositions comprising prebiotics and micronutrients. More particularly, the application relates to oral compositions comprising prebiotics, beta-glucan and micronutrients and the process of preparation for the same. The present application further relates to a nutritional composition in the form of gummies and process for preparation thereof.

NUTRACEUTICAL COMPOSITION FOR ORAL ADMINISTRATION

FIELD OF THE APPLICATION

[001] The present application relates to a oral composition comprising nutrients to address the nutrition deficiency in human subjects. Particularly the application relates to oral compositions comprising prebiotics and micronutrients. More particularly, the application relates to oral compositions comprising prebiotics, beta-glucan and micronutrients and the process of preparation for the same.

BACKGROUND

[002] Regular dietary intake of various essential nutrients is recommended for healthy and balanced nutrition. Appropriate daily intake of these nutrients is extremely necessary as deficiency of these nutrients leads to several diseases. Macronutrients like carbohydrates and fats have important role in energy production, whereas proteins have role in maintaining tissue structure, hormone system, enzyme systems which regulate various metabolic activities. Micronutrients have many important functions which are ultimately connected to the growth and development of the body. Dietary fiber intake is important for maintaining health of the digestive track. Deficiency of nutrients in diet may lead to various health issues and sometimes major health concerns if the health issues left untreated for a longer duration of time. Lack of proper nutrition ultimately leads to weakened immune system and consequent negative effects on physical and mental health of a person.

[003] In today's fast pace of life, it becomes difficult to ensure that daily diet contains all the nutrients in adequate amounts. Hence, to address the issue of deficit of nutrients in daily diet, consumption of dietary nutritional supplements becomes important.

[004] Iron is an essential mineral in body functioning. It is particularly important in keeping red blood cells healthy. Nearly, 70% of the trusted source of the iron in the body is located in the hemoglobin. When the body lacks adequate amount of iron, production of hemoglobin is reduced thus making humans susceptible to many diseases. This condition is called as iron deficiency anemia (IDA) and can be treated by consuming iron rich nutrients as required.

[005] The main causes of this insufficiency could be lack of iron-rich foods in the diet or inability of the body to absorb ingested iron owing to acquired or genetic causes. Iron deficiency (ID) affects about 40% of the population in developing countries and around 10% of the inhabitants of developed countries. Iron supplements and iron-fortified foods are commonly used in children to prevent ID. However, literature also states that iron alters development of the gut microbiota in children. Unabsorbed iron in the gut may exert detrimental effects on the microbiota. The developing microbiota confers multiple health benefits, such as improved intestinal barrier function and nutrient absorption, as well as infection resistance. Further, undesirable effects on the gut microbiota due to unabsorbed iron could be a causative factor for reduced immunity and low iron status in children.

[006] Present application aims to address the above issues, and provide a nutraceutical composition that comprises of prebiotics that support healthy gut microbiota along with essential micronutrients including iron in adequate amounts.

[007] The nutraceutical composition disclosed by the present application helps to maintain the daily levels of nutrients in body along with the added health benefits associated with its components like beta-glucan and selenium.

[008] The nutraceutical composition is well accepted if it is provided in compact, consumer friendly dosage form with acceptable organoleptic properties and requires less time in consumption and minimum number of doses per day which ultimately leads to positive nutritional effects and improves the health.

[009] Generally, most children have difficulty in swallowing traditional solid dosage forms (e.g., tablets and capsules) at least until the age of five due to the risk of choking. For young children (i.e., <4 years of age), liquid dosage forms are preferred, as dosing can be facilitated with a spoon or oral syringe. However, liquid formulations can be problematic as they enhance the bitter taste of active ingredients in solution.

[0010] Alternative non-liquid formulations have been designed to compensate for the poor dosing acceptability and taste limitation of liquid-based formulations for older children (>2 years of age). These formulations typically can include chewable tablets, gummies, lollipops, and other confectionary mimics.

[0011] Gummy dosage forms are particularly effective for enabling compliant dosing in children as they provide a palatable, chewable base and can incorporate active ingredient(s) that are generally of very low dose, have the ability to withstand the high thermal stress of the gummy manufacturing process, and have low intrinsic taste response. Moreover, while gummy dosage forms provide the basis for effective dosing of active ingredients to children, their application for the delivery of nutrients and like materials has been highly restrictive due to the compatibility, formulation and stability challenges associated with the gummy dosage form.

[0012] Hence, the present application relates to a easy to consume oral composition which contains a unique combination of essential nutrients and is having the desired stability. The composition aims to provide an effective amount of prebiotics and micronutrients through minimum number of doses per day, and thereby help to prevent the health issues which may arise out of nutritional deficiencies.

[0013] The composition taught by the present application intends to address the nutritional deficiencies in diet with a easy to consume oral unit composition thereby minimizing or eliminating the need to ingest separate nutritional supplements for each component in order to fulfil the dietary requirements of essential nutrients.

SUMMARY OF THE APPLICATION

[0014] The primary object of the present application is to provide a novel blend of prebiotic, beta-glucan and essential micronutrients for oral administration in order to satisfy the daily nutritional requirements of human body and thereby improve the overall immune system.

[0015] Another object of the present application is to provide an oral nutraceutical composition comprising: a prebiotic component; a beta glucan; a micronutrient component comprising vitamins and minerals; and one or more nutraceutically acceptable excipients.

[0016] Another object of present application is to provide an oral nutraceutical composition comprising prebiotic, beta-glucan and essential micronutrients in the form of gummies, wherein the composition further comprises iron, zinc, and selenium.

[0017] Another object of the present application is to provide an easy to consume, oral composition comprising a prebiotic component selected from fructans, Fructo-oligosaccharides (FOS), galacto-oligosaccharides (GOS), trans-galacto-oligosaccharides (TOS), starch, glucose-derived oligosaccharides, pectic-oligosaccharides, cocoa-derived flavonol or combinations thereof.

[0018] One additional object of the present application is to provide an oral composition comprising a beta-glucan obtained from natural sources such as barley, oats, rye, wheat, yeast or combinations thereof.

[0019] Another object of the present application is to provide a chewable oral composition comprising a prebiotic component in an amount from 20% w/w to 40% w/w; and beta-glucan in an amount from 0.5% w/w to 5% w/w of the total composition.

[0020] Another object of the present application is to provide an easy to consume, oral composition comprising prebiotic component and the beta-glucan in the ratio of 40:0.75 to 30:1.5.

[0021] Another object of the present application is to provide an oral composition comprising micronutrient in an amount from 0.5 % to 8 % w/w of the total composition.

[0022] Another object of the present application is to provide an oral composition comprising one or more minerals selected from iron, zinc and selenium in an amount from 0.15% w/w to 2.5 % w/w of the total composition.

[0023] Another object of the present application is to provide an oral composition comprising Iron in an amount from 0.05 % to 0.5 % w/w of the total composition.

[0024] Another object of the present application is to provide an oral composition that provides an energy density of from 2 kcal/g to 10 kcal/g of the composition.

[0025] Another object of the present application is to provide a method for improving the immunity in pediatric subjects, wherein said method comprises administersing an oral nutraceutical composition comprising:

a prebiotic component;
a beta glucan;
a micronutrient component comprising vitamins and minerals; and
one or more nutraceutically acceptable excipients.

[0026] Another object of the present application is to provide a method for improving the immunity in pediatric subjects, wherein said method comprises administersing an oral nutraceutical composition comprising a prebiotic component in an amount from 20% w/w to 40% w/w; and beta-glucan in an amount from 0.5% w/w to 5% w/w of the total composition.

[0027] Another object of the present application is to provide a method for improving the immunity in pediatric subjects, wherein said method comprises administersing an oral nutraceutical composition comprising the prebiotic component and the beta-glucan in the ratio of 40:0.75 to 30:1.5.

[0028] Another object of the present application is to provide a method for improving the immunity in pediatric subjects, wherein said method comprises administersing an oral nutraceutical composition comprising a prebiotic component in an amount from 20% w/w to 40% w/w; and beta-glucan in an amount from 0.5% w/w to 5% w/w of the total composition, and wherein said composition modulates the levels of immunity markers in the biological fluids of the subject by atleast 5% to 25% when compared to the baseline levels.

[0029] Another object of the present application is to provide a method for improving the immunity in pediatric subjects, wherein said method comprises administersing an oral nutraceutical composition comprising a prebiotic component in an amount from 20% w/w to 40% w/w; and beta-glucan in an amount from 0.5% w/w to 5% w/w of the total composition, and wherein said composition increases the heamoglobin levels in the subject by atleast 5% to 20% when compared to the baseline levels.

[0030] Another object of the present application is to provide an oral composition wherein the composition is a tablet, capsule, granules, pellets, jelly, chewable tablets, gummies, lollipops, and other confectionary mimics.

[0031] The various embodiments herein disclose oral nutraceutical composition in the form of gummy composition and process of preparation of the same.

[0032] Other objects and advantages of the present application will become apparent to those skilled in the art upon reading the following detailed description of the preferred embodiments.

DETAILED DESCRIPTION OF THE APPLICATION

[0033] The details of one or more embodiments of the present invention are set forth in this document. Modifications to embodiments described in this document and other embodiments will be evident to those of ordinary skill in the art after studying the information provided in this document. The information provided in this document, particularly the specific details of the described exemplary embodiments, is provided primarily for clear understanding, and no unnecessary limitations are to be understood therefrom.

[0034] Unless otherwise defined, all technical and scientific terms used herein have the same meaning as commonly understood by a person having an ordinary skill in the art.

[0035] The present application teaches a novel composition that combines the properties of beta-glucan and selenium along with micronutrients and probiotic component which aims to address the nutritional deficiencies in human diet in a holistic manner.

[0036] **Definitions:** The terms as used herein have the following meanings:

[0037] The term "comprising" is “open-ended” and means the elements recited, or their equivalent in structure or function, plus any other element or elements which are not recited. The terms "having" and "including" are also to be construed as open-ended unless the context suggests otherwise. These terms are not in the exclusive sense of "consisting only of". All ranges recited herein include the endpoints, including those that recite a range "between" two values.

[0038] The terms "a" and "the" as used herein are understood to encompass the plural as well as the singular or otherwise clearly mentioned wherever needed. For example, “an excipient” includes one or more of such excipients.

[0039] As used herein, “about”, “up to” is understood to refer to numbers in a range of numerals. Moreover, all numerical ranges herein should be understood to include all integers, whole or fractions, within the range.

[0040] As used herein, the term “at least” refers to the presence of the recited substance in the composition in recited least amount.

[0041] The terms “excipient” or “additives” are used interchangeably to mention any safe food acceptable material or a component of the composition that is not having any pharmacological effect, which is acceptable for use in nutritional compositions and does not provide any therapeutic effect, and may contribute to physicochemical properties or any relevant nontherapeutic function of the composition. The excipients that are useful in preparing a nutritional composition are generally safe, non-toxic, do not interact with other components of a composition in a deleterious manner, and are acceptable for human or veterinary use. As used in the specification, the term "excipient" includes both one and more than one such excipient.

[0042] The terms “composition” and “formulation” are used interchangeably and refer to a mixture of two or more components, elements, or fractions. Also, the terms “composition” and “formulation” may be used to refer to a mixture of the components with excipients or other carriers. The nutritional compositions in the present application are selected from but are not limited to tablets, chewable tablets, capsules, jelly, gummies, lollipops, and other confectionary mimics..

[0043] "Children" or “Paediatric” means a subject ranging in age from about 2 years to about 18 years. In other embodiments, the terms "children" or "child" or “adolescent” refer to any range of ages between about 24 months and about 18 years.

[0044] "Children's nutritional product" refers to a composition that satisfies at least a portion of the nutrient requirements of a paediatric subject.

[0045] The term, "effective amount" is an amount that prevents a deficiency, treats a disease or medical condition in an individual, or, more generally, reduces symptoms, manages progression of the diseases, or provides a nutritional, physiological, or medical benefit to the individual. Treatment can be patient- or doctor-related.

[0046] The term "dietary insufficiencies" refer to the deficit in the amount of recommended intake of a particular nutrient.

[0047] While the terms "subjects," "individual," and "patient" are used herein to refer to a human, the application is not so limited. Accordingly, the terms "individual" and "patient" refer to any animal, mammal, or human having or at risk for a medical condition that can benefit from or may need the nutritional composition as described herein in the present application.

[0048] The term "Gummies" means and includes the products intended for oral administration that contain the active ingredient(s) along with suitable excipient(s) and which is expected to be chewed before swallowing. Unlike chewing gums the discomfort caused by 'gum cud' is avoided in case of gummies as gummies are meant to be ingested and all the components of gummies are edible and fully digestible.

[0049] The term "immunity" as described herein indicates all of the physiological mechanisms that enable an individual's body to recognize materials as foreign and to neutralize, eliminate, or metabolize them without injury to its own tissue.

[0050] The term "immunity boosting" as used herein denotes all the factors and/or the component(s)/ingredients(s) and/or compositions of the ingredient(s) which help the body to give effective immunity or immune response thereby strengthening the defence system by fulfilling the unmet needs of various nutrients in the body of the subject.

[0051] "Nutritional compositions" or "Nutraceutical preparation" or "Nutraceutical composition" as used herein, are understood to include one or more of the dietary nutrients as components and any number of additional optional ingredients, including but are not limited to conventional food additives, health benefit additives, one or more, acidity regulators, thickening/gelling agents, buffers or agents for pH adjustment, chelating agents,

colorants, flavorants, emulsifiers, mineral osmotic agents, pharmaceutically acceptable carrier, preservatives, anti-oxidants, stabilizers, sweeteners, texturizers. The optional ingredients can be added in any suitable amount. "Nutritional composition" further means a substance or composition that satisfies at least a portion of a subject's nutrient requirements.

[0052] As far as the present application is concerned the terms “Nutritional compositions” or “Nutraceutical preparation” or “Nutraceutical composition” are used interchangeably with “Immunity boosting nutritional compositions” or “Immunity boosting nutraceutical preparation” or “Immunity boosting nutraceutical composition” respectively. The “immunity boosting” nature of the preparations/compositions described by the present application is attributed to the novel blend of nutrients as presented by the present application.

[0053] The term “protein”, as used herein, is understood to refer to any food component that includes single amino acid (monomer), two or more amino acids joined together by a peptide bond (dipeptide, tripeptide, or polypeptide), collagen, precursor, homolog, analog, mimetic, salt, prodrug, metabolite, or fragment thereof or combinations thereof. For the sake of clarity, the use of any of the above terms is interchangeable unless otherwise specified.

[0054] Non-limiting examples of proteins include, but are not limited to dairy-based proteins, plant-based proteins, animal-based proteins, and artificial proteins. Dairy-based proteins include, for example, casein, caseinates (e.g., all forms including sodium, calcium, potassium caseinates), casein hydrolysates, whey (e.g., all forms including concentrate, isolate, demineralized), whey hydrolysates, milk protein concentrate, and milk protein isolate. Plant-based proteins include, for example, soy protein (e.g., all forms including concentrate and isolate), pea protein (e.g., all forms including concentrate and isolate), canola protein (e.g., all forms including concentrate and isolate), other plant proteins that commercially are wheat and fractionated wheat proteins, corn and its fractions including zein, rice, oat, potato, peanut, green pea powder, green bean powder, and any proteins derived from beans, lentils, pulses and the like or combinations thereof.

[0055] The term “fats or lipids” is construed as per their general meaning and includes but is not limited to one or more short-chain fatty acid(s), medium-chain fatty acid(s), long-chain fatty acid(s), monounsaturated fatty acid(s), and/or mixtures thereof.

[0056] The term “carbohydrate” is construed as per its general meaning and includes but is not limited to sorbitol, xylitol, or maltitol, trehalose, maltodextrin, processed starch, amylose starch, tapioca starch, fructose, lactose, and the like or mixtures thereof.

[0057] The term “fiber” is construed as per its general meaning and includes but is not limited to a dietary fiber, or any mixture of dietary fibers; more preferably one or more of fructo-oligosaccharides, soluble non-starch polysaccharides, insoluble non-starch polysaccharides, non-digestible oligosaccharides, inulin, acacia fiber, arabic gum, soy polysaccharide, alpha-cellulose, resistant starch, and the like or mixtures thereof.

[0058] The term “vitamin” includes but is not limited to any of various fat-soluble or water-soluble organic substances essential in minute amounts for normal growth and activity of the body and obtained naturally from plant and animal foods or synthetically made, pro-vitamins, derivatives, analogs and the like mixtures thereof.

[0059] Non-limiting examples of vitamins include vitamin A, vitamin B1(thiamine), vitamin B2 (riboflavin), vitamin B3 (niacin or niacinamide), vitamin B5 (pantothenic acid), vitamin B6 (pyridoxine, pyridoxal, or pyridoxamine, or pyridoxine hydrochloride), vitamin B7 (biotin), vitamin B9 (folic acid), and vitamin B12 (various cobalamins; commonly cyanocobalamin in vitamin supplements), vitamin C, vitamin D, vitamin E, vitamin K, and the like mixtures thereof.

[0060] “Vitamin Premix” is the mixture containing two or more of the vitamins and any additional excipients. More preferably it comprises of ingredients that include but are not limited to Retinyl Acetate, Cholecalciferol, D-alpha tocopheryl acetate, Pyridoxine Hydrochloride, Folic acid, Cyanocobalamin, L-Ascorbic acid, and the like mixtures thereof.

[0061] The term “mineral” includes but is not limited to one or more minerals selected from boron, calcium, chromium, copper, iodine, iron, magnesium, manganese, molybdenum,

nickel, phosphorus, potassium, selenium, silicon, tin, vanadium, zinc, and the like or mixtures thereof.

[0062] "Mineral Premix" is the mixture containing two or more of the minerals and any additional excipients. More preferably it comprises of ingredients that include but are not limited to Zinc Sulphate monohydrate, Ferric sodium di-phosphate, Sodium Selenite, and the like or mixtures thereof.

[0063] The term "antioxidant" includes but is not limited to any one or more of various substances such as beta-carotene (a vitamin A precursor), vitamin C, vitamin E, and selenium that inhibit oxidation or reactions promoted by reactive oxygen species ("ROS") and other radical and non-radical species. Additionally, antioxidants are molecules capable of slowing or preventing the oxidation of other molecules.

[0064] Non-limiting examples of antioxidants include carotenoids, Ascorbyl Palmitate, coenzyme Q10 ("CoQ10"), flavonoids, glutathione Goji (wolfberry), hesperidin, lactowolfberry, lignan, lutein, lycopene, polyphenols, selenium, vitamin A, vitamin B1, vitamin B6, vitamin B12, vitamin C, vitamin D, vitamin E, zeaxanthin, and the like or mixtures thereof.

[0065] The term "acidity regulator" denotes the substances which are used to control and alter the acidity or alkalinity of the product; maintain desired pH which is necessary to maintain colour, flavour, taste and texture of the product and help in natural preservation of the product. These include but are not limited to acetic acid, citric acid, trisodium citrate, malic acid, fumaric acid, lactic acid, tartaric acid, succinic acid, phosphoric acid, and the like or mixtures thereof.

[0066] The term "gelling agent" denotes the substances that are gel-forming agents when dissolved in a liquid phase as a colloidal mixture form a weakly cohesive internal structure and which are responsible to enhance the thickness or viscosity of the composition. These include but are not limited to natural gelling agents (like gelatin, casein, collagen, polysaccharides like guar gum, acacia, tragacanth, bug bean gum, pectin, starch, xanthan gum, dextran, succinoglucan etc.) and Semisynthetic gelling agents (like carboxymethyl

cellulose, ethylcellulose, hydroxyethyl cellulose, hydroxypropyl cellulose, methylcellulose, sodium alginate etc.), and the like or mixtures thereof.

[0067] The term "Prebiotics" denotes the substrates for gut micro-organisms which ultimately confers several health benefits. Prebiotics are fermented by gut bacteria to produce short-chain fatty acids (SCFAs), hydrogen and carbon dioxide. Prebiotics affect gut health by altering the composition of the gut microbiome and by increasing the production of short chain fatty acids. They stimulate the growth of beneficial microbes in the gut, shifting the overall microbiome to a more positive composition. An increase in the number of friendly bacteria, further promotes the production of SCFAs which in turn reduce colonic luminal pH. A healthy microbiome is also associated with improved mucosal barrier integrity as the presence of friendly bacteria in the gut exert a 'barrier effect', protecting the gut lining from damage and increased permeability. Prebiotics can further be used to supplement the diet of paediatric subjects.

[0068] The term "prebiotic" includes the substances which are non-digestible food ingredients that beneficially affect the host by selectively stimulating the growth and/or activity of one or a limited number of bacteria in the colon, and thus improves host health. Non-limiting examples of sources of prebiotics are various cereals, vegetables, and fruits like barley, oats, wheat, asparagus, chicory, sugar beet, soy bean, banana, flaxseeds etc. Prebiotics can be carbohydrates or non-carbohydrate compounds. Carbohydrate-prebiotics include compounds like fructans, galacto-oligosaccharides, starch and glucose-derived oligosaccharides and pectic oligosaccharides etc. whereas non-carbohydrate prebiotics include cocoa-derived flavanols. The prebiotics used in this application include but are not limited to Fructo-oligosaccharides (FOS), galacto-oligosaccharides (GOS) and trans-galacto-oligosaccharides (TOS).

[0069] The term "Beta-glucans" comprise a group of β-D-glucose polysaccharides naturally occurring in the cell walls of cereals, bacteria, and fungi. Beta-glucans are soluble fibres found in the family of grasses (*Gramineae*) such as barley, oats, rye, and wheat. Beta-glucans obtained from various natural sources have been found to have various health benefits. Barley and oats beta-glucans have been reported to reduce the risk of cardiovascular disease by decreasing circulating blood cholesterol. Similarly, beta-glucans

obtained from yeast have been found to have important role in strengthening the immune system.

[0070] "Per serve" or "per unit" or "per serving" as per the present application refers to the recommended daily serving in terms of number of units consumed. Per serve can refer to 1 unit, 2 units, 3 units, 4 units or 5 units that are recommended to be consumed daily.

[0071] The term the immunity markers as used herein can include, but are not limited to one or more of the Natural Killer cell (NK cell) activity, Immunoglobulin (IgA, IgE), Absolute Neutrophil Count (ANC), C-Reactive Protein (CRP) and combination thereof as measured thorough biological sample analysis.

[0072] The term Baseline or Base level /value as used herein refers to any of one or more physiological, or biological parameters of the subject as measured at the beginning of enrollment into the clinical study, and represent the levels of the parameters measured before administration or consumption of the composition of this application.

[0073] Present application relates to a nutraceutical composition for oral use which contains a novel blend of micronutrients that are compatible with each other. More specifically it is a unique combination of essential micronutrients including selenium and further comprises of beta-glucan.

[0074] Present application relates to a unit composition which is unique blend of nutraceutically effective ingredients like beta-glucan, prebiotic and essential vitamins and minerals having positive effects with respect to the immunity building in human body. The combination of these ingredients has found to be useful for both adults and paediatric subjects.

[0075] Because both the interaction among dietary components and among the microflora of the intestinal ecosystem are very complex, the composition of the paediatric nutritional supplement may influence the effectiveness of prebiotics and oligosaccharides when such ingredients are provided as supplements in the diet of a child. Moreover, the type and concentration of the components used in a composition may also modulate the intestinal microbiota.

[0076] Accordingly, it would be beneficial to provide a nutritional composition for paediatric subjects comprising a nutritional supplement that stimulates the immune system, wherein the supplement is provided in an easy to administer oral jelly or gummy form that is appealing to the children or paediatric subjects in general. Furthermore, it would be beneficial to provide methods for enhancing and improving the immune response of a paediatric subject via administration of a nutritional composition that is well- tolerated by paediatric subjects.

[0077] The gut microflora of the paediatric subjects is well known to be less developed than that of an adult. While the microflora of the adult human consists of more than millions microorganisms and more than 550 species, the gut microflora of a child contains only a fraction of it, both in terms of number and variety of species. Because the bacterial populations and species vary immensely between the gut of a child and an adult, it cannot be assumed that a prebiotic substance that has a beneficial effect on adults would also have a beneficial effect on infants and/or children.

[0078] As mentioned earlier, beta-glucans are β-D-glucose polysaccharides naturally occurring in the cell walls of cereals, bacteria, and fungi, with significantly different physicochemical properties dependent on source. The chemical structure of beta-glucans depends on the source of the glucan. Moreover, various physiochemical parameters, such as solubility, primary structure, molecular weight, and branching, play a role in biological activities of beta-glucan.

[0079] Beta-glucans obtained from yeast have been found to support the immune system and can help to fight infections, while also showing anticarcinogenic effects. Adults with susceptible immune systems had a reduction in upper respiratory tract infections following beta-glucan supplementation. Beta-glucans obtained from cell wall of yeast (*Saccharomyces cerevisiae)* have been reported to reduce the inflammatory effects of cytokines by elevating the anti-inflammatory cytokines after exposing the pigs to an immunological challenge.

[0080] In the preferred embodiments of the present application, beta-glucan is Wellmune®. Wellmune® is a proprietary food, beverage and supplement ingredient of Kerry Group PLC. Wellmune® is a beta-glucan which is a naturally occurring polysaccharide derived from

cell wall of baker's yeast (*Saccharomyces cerevisiae*) and is a self-affirmed generally recognized as safe (GRAS). Wellmune® improves the functioning of the innate immune system by making key white blood cells (specifically called leukocytes) better able to find and kill potential pathogens. Studies have shown that Wellmune® has ability to reduce the duration and severity of upper respiratory tract symptoms.

[0081] As noted, glucans are polysaccharides that belong to a group of physiologically active compounds described as biological defense modifiers. Beta-glucans are a polysaccharide fraction that strengthen the immunity, which may decrease microbial-related illnesses in children by stimulating immune function when administered as part of the nutritional composition of the present disclosure. The efficacy of beta-glucan as an immune system stimulator has not previously been demonstrated when the beta-glucan is administered simultaneously with micronutrients in order to provide a synergistic, stimulatory immune effect.

[0082] In some embodiments, the nutritional composition of the present disclosure comprises beta-glucan together with specific micronutrients, wherein the combination of these ingredients provides a synergistic effect when incorporated in a nutritional composition. In some embodiments, the combination of beta-glucan with specific micronutrients provides the effect of increasing the neutrophils count and respiratory capacity in a subject.

[0083] In one embodiment, the nutritional composition comprising beta-glucan together with specific micronutrients for a paediatric subject, will improve the subject's immune response by increasing resistance against invading pathogens and therefore maintaining or improving overall health. Beta-glucan is able to induce a response by cells of the immune system.

[0084] Additionally, in some embodiments, the use of beta-glucan enhances immune system function. For example, the use of beta-glucan may enhance resistance to infection and/or reduce inflammatory responses. In at least one embodiment, the present disclosure is directed to a method for enhancing the immune system function in a paediatric subject comprising administering to the subject a beta-glucan in a jelly or gummy composition. In another embodiment, the present disclosure is directed to a method for enhancing resistance

to infection in a paediatric subject comprising administering to the subject a beta-glucan together with specific micronutrients in a jelly or gummy composition.

[0085] In still another embodiment, the present disclosure is directed at a method for reducing the duration and severity of infection caused by a broad spectrum of bacterial and viral pathogens in a paediatric subject comprising administering to a paediatric subject a beta-glucan together with specific micronutrients.

[0086] Selenium is a trace element which is necessary for the biosynthesis of selenoenzymes and selenoproteins such as glutathione peroxidase, thioredoxin reductase, iodothyronine deiodinase, and selenoprotein W and P, respectively. They mediate an array of activities such as antioxidant defense, detoxification, anti-inflammation, immunomodulation, carcinogenesis prevention, thyroid functioning, and sperm motility and maturation, thyroid hormone metabolism, and DNA synthesis.

[0087] Iron is an essential mineral in body functioning. It is particularly important in keeping red blood cells healthy. When the body lacks adequate amount of iron, production of hemoglobin is reduced thus making humans susceptible to many diseases. This condition is called as iron deficiency anemia (IDA) and can be treated by compensation of the dosage externally. Few sources include but are not limited to iron rich food, food fortified with ferrous sulfate, Ferric sodium di-phosphate, Ferric sodium phosphate, ferrous fumarate, ferric pyrophosphate and and the like or mixtures thereof.

[0088] Zinc is an essential mineral having catalytic activity of several enzymes, and it plays a role in enhancing immune function, protein and DNA synthesis, wound healing, and cell signaling and division. Zinc also has a role in lipid and glucose metabolism regulating and forming the expression of insulin. Zinc is necessary for healthy growth and development during pregnancy, infancy, childhood, and adolescence as well.

[0089] Present application relates to a unique combination which attempts to combine the health benefits of beta-glucan, prebiotics and essential nutrients in a single unit dose composition to achieve a synergistic positive effect on human immunity thereby minimizing the need of taking individual nutritional supplements for immunity enhancement.

[0090] The present application also describes a method of enhancing the immune function of a paediatric subject comprising administering an effective amount of a nutritional composition comprising a carbohydrate source, a lipid source, a protein source and a source of beta-glucan.

[0091] In an embodiment, the nutritional composition comprises of one or more of proteins, fats or lipids, fibers and carbohydrates.

[0092] In an embodiment, the nutritional composition comprises of a carbohydrate fraction present in an amount of about 30 % to about 90% w/w of the composition.

[0093] In an embodiment, the nutritional composition comprises of a sugar base in an amount from 20 % to 90 % w/w of the total composition.

[0094] In an embodiment, the nutritional composition comprises of a sugar base in an amount from 25 % to 85 % w/w of the total composition.

[0095] In an embodiment, the nutritional composition comprises a sugar base in an amount from 30 % to 80 % w/w of the total composition.

[0096] In an embodiment, the nutritional composition comprises a sugar base in an amount from 35 % to 75 % w/w of the total composition.

[0097] In an embodiment, the nutritional composition comprises of a protein fraction present in an amount of about 1% to about 5% w/w of the composition.

[0098] In an embodiment, the nutritional composition comprises of a protein fraction present in an amount of about 2% to about 4% w/w of the composition.

[0099] In an embodiment, the nutritional composition comprises of protein fraction present in an amount of about 2.5% to about 3.5% w/w of the composition.

[00100] In an embodiment, the nutritional composition comprises of a fat fraction present in an amount of about 0% to about 1.0 % w/w of the composition.

[00101] In an embodiment, the nutritional composition comprises one or more prebiotics.

[00102] In an embodiment, the probiotic component is selected from a group of compounds including but are not limited to Fructo-oligosaccharides (FOS), galacto-oligosaccharides (GOS), and trans-galacto-oligosaccharides (TOS).

[00103] In an embodiment, the prebiotic component is a Fructo-oligosaccharide (FOS).

[00104] In an embodiment, the nutritional composition comprises a prebiotic component in an amount of about 20 % to 40% w/w of the composition.

[00105] In an embodiment, the nutritional composition comprises a prebiotic component in an amount of about 22 % to 38% w/w of the composition.

[00106] In an embodiment, the nutritional composition comprises a prebiotic component in an amount of about 24 % to 36% w/w of the composition.

[00107] In an embodiment, the nutritional composition comprises a prebiotic component in an amount of about 25 % to 35% w/w of the composition.

[00108] In an embodiment, the nutritional composition comprises a prebiotic component in an amount of about 26 % to 34% w/w of the composition.

[00109] In an embodiment, the nutritional composition further comprises beta-glucan or combinations thereof.

[00110] In an embodiment, the nutritional composition comprises beta-glucan in an amount of about 0.5% to 5% w/w of the composition.

[00111] In an embodiment, the nutritional composition comprises beta-glucan in an amount of about 1% to 4% w/w of the composition.

[00112] In an embodiment, the nutritional composition comprises beta-glucan in an amount of about 1.5% to 3% w/w of the composition.

[00113] In an embodiment, the nutritional composition comprises beta-glucan in an amount of about 2% to 3% w/w of the composition.

[00114] In some embodiments, the nutritional composition comprises between about 25mg and about 200mg beta-glucan per serving. In another embodiment, the nutritional composition comprises between about 30mg and about 150mg beta-glucan per serving. In another embodiment, the nutritional composition comprises between about 40mg and about 100 mg beta-glucan per serving. In other embodiments, the nutritional composition comprises an amount of beta-glucan sufficient to provide upto 100mg beta -glucan per day. In some embodiments, beta-glucan may be added to the nutritional composition at a concentration sufficient to deliver a target of upto 80 mg of beta-glucan per day to a subject. The nutritional composition may be delivered in multiple doses to reach a target amount of beta-glucan delivered to the subject throughout the day.

[00115] In an embodiment, the nutritional composition further comprises beta-glucan or combinations thereof wherein beta-glucan is preferably sourced from the baker's yeast.

[00116] In an embodiment, the nutritional composition further comprises beta-glucan or combinations thereof wherein beta-glucan is preferably Wellmune®.

[00117] In an embodiment, the probiotic component in the nutritional composition is a fiber component.

[00118] In an embodiment, the nutritional composition comprises a prebiotic and beta-glucan components wherein prebiotic component and the beta-glucan are present in the ratio of 40:0.5 to 20:0.5

[00119] In an embodiment, the nutritional composition comprises a prebiotic and beta-glucan components wherein prebiotic component and the beta-glucan are present in the ratio of 40 :0.75 to 30:1.5

[00120] In an embodiment, the nutritional composition comprises a prebiotic and beta-glucan components wherein prebiotic component and the beta-glucan are present in the ratio of 38 :1 to 20:1.

[00121] In an embodiment, the nutritional composition comprises a prebiotic and beta-glucan component wherein prebiotic component and the beta-glucan are present in the ratio of 30:1 to 15:1.

[00122] In an embodiment, the nutritional composition comprises a micronutrient portion comprising one or more of vitamins, minerals, and additives.

[00123] In an embodiment, the nutritional composition comprises a micronutrient portion in an amount from 0.25 % to 10 % w/w of the total composition.

[00124] In an embodiment, the nutritional composition comprises a micronutrient portion in an amount from 0.5 % to 8 % w/w of the total composition.

[00125] In an embodiment, the nutritional composition comprises a micronutrient portion in an amount from 0.75 % to 6 % w/w of the total composition.

[00126] In an embodiment, the nutritional composition comprises a micronutrient portion in an amount from 1 % to 4 % w/w of the total composition.

[00127] In an embodiment, the nutritional composition comprises a micronutrient portion in an amount from 1.25 % to 2 % w/w of the total composition.

[00128] In an aspect of the above embodiment, said micronutrient component comprises one or more minerals selected from iron, zinc and selenium in an amount from 0.15 % w/w/ to 2.5 %w/w of the total composition.

[00129] In an embodiment, the nutritional composition comprises iron in an amount from 0.05 % to 0.5 % w/w of the total composition.

[00130] In an embodiment, the nutritional composition comprises iron in an amount from 0.06 % to 0.3 % w/w of the total composition.

[00131] In an embodiment, the nutritional composition comprises one or more vitamins selected from vitamin A (retinol), vitamin B1 (thiamine), vitamin B2 (riboflavin), vitamin B3 (niacin), vitamin B5 (pantothenic acid), vitamin B6 (pyridoxine), vitamin B8 (biotin), vitamin B9 (folic acid), vitamin B12 (cyanocobalamin), vitamin C (ascorbic acid), vitamin D2 (ergocalciferol), vitamin D3 (cholecalciferol), vitamin E (alpha-tocopherol), vitamin K and, and the like or mixtures thereof.

[00132] In an embodiment, the nutritional composition comprises one or more minerals selected from boron, calcium, chromium, copper, iodine, iron, magnesium, manganese, molybdenum, nickel, phosphorus, potassium, selenium, silicon, tin, vanadium, zinc, and the like or mixtures thereof.

[00133] In an embodiment, the nutritional composition comprises a micronutrient portion which comprises of a vitamin premix and mineral premix comprising one or more vitamins and one or more minerals respectively.

[00134] In an embodiment, the nutritional composition comprises a micronutrient portion comprising of a vitamin premix and mineral premix in the range of the ratio of 1:6 to 6:1.

[00135] In an embodiment, the nutritional composition comprises a micronutrient portion comprising of a vitamin premix and mineral premix in the range of the ratio of 2:5 to 5:2.

[00136] In an embodiment, the nutritional composition comprises a micronutrient portion comprising of a vitamin premix and mineral premix in the ratio of 1:2 to 2:1.

[00137] In an embodiment, the nutritional composition comprises a mineral portion wherein selenium and zinc are in the range of the ratio of 0.001:5 to 0.005:1.

[00138] In an embodiment, the nutritional composition comprises a mineral portion wherein selenium and zinc are in the range of the ratio of 0.002:4 to 0.004:2

[00139] In an embodiment, the nutritional composition comprises a mineral portion wherein selenium and zinc are in the ratio of 0.0025:3 to 0.0035:2

[00140] In an embodiment, the nutritional composition further comprises antioxidants.

[00141] In an embodiment, the nutritional composition comprises antioxidants which can be selected from but are not limited to carotenoids, Ascorbyl Palmitate, coenzyme Q10 ("CoQ10"), flavonoids, glutathione Goji (wolfberry), hesperidin, lactowolfberry, lignan, lutein, lycopene, polyphenols, selenium, vitamin A, vitamin B1, vitamin B6, vitamin B12, vitamin C, vitamin D, vitamin E, zeaxanthin, and the like or mixtures thereof.

[00142] In an embodiment, the nutritional composition further comprises acidity regulator.

[00143] In an embodiment, the nutritional composition comprises acidity regulator which is selected from but is not limited to acetic acid, citric acid, trisodium citrate, malic acid, fumaric acid, lactic acid, tartaric acid, succinic acid, phosphoric acid, and the like or mixtures thereof.

[00144] In an embodiment the nutritional composition further comprises colourant.

[00145] In an embodiment the nutritional composition comprises colourant which can be natural colour or permitted synthetic colour.

[00146] In an embodiment, the nutritional composition comprises is used for oral administration.

[00147] In another aspect of the present application, the oral nutritional composition is a tablet, chewable tablet, capsule, jelly or gummy composition for direct oral consumption.

[00148] In an aspect of above embodiment, the gummies have base material comprising of a gelling agent.

[00149] In an aspect of above embodiment, the gelling agent acts as an emulsifying and stabilizing agent.

[00150] In an aspect of above embodiment, the gelling agent is selected from but is not limited to natural gelling agents (like gelatin, casein, collagen, polysaccharides like guar gum, acacia, tragacanth, bug bean gum, pectin, starch, xanthan gum, dextran, succinoglucan etc.) and Semisynthetic gelling agents (like carboxymethyl cellulose, ethylcellulose, hydroxyethyl cellulose, hydroxypropyl cellulose, methylcellulose, sodium alginate etc.), and the like or mixtures thereof.

[00151] In an aspect of above embodiment, the gelling agent is obtained from pectin.

[00152] In an embodiment, the nutritional composition provides an energy density of between 2 kcal to 15 kcal per unit.

[00153] In an embodiment, the application relates to the use of the nutritional composition as food or nutritional supplement that helps in improving immunity, wherein the improvement in immunity is marked or assessed by modulation in the levels of immunity markers when assessed through biological parameter and related testings.

[00154] In an embodiment, the application relates to method of improving the immunity in pediatric subjects, wherein said method comprises administersing an oral nutraceutical composition comprising:

a prebiotic component;

a beta glucan;

a micronutrient component comprising vitamins and minerals; and

one or more nutraceutically acceptable excipients.

[00155] In an embodiment, the application relates to method of improving the immunity in pediatric subjects, wherein said method comprises administersing an oral nutraceutical

composition comprising a prebiotic component in an amount from 20% w/w to 40% w/w; and beta-glucan in an amount from 0.5% w/w to 5% w/w of the total composition.

[00156] In an embodiment, the application relates to method of improving the immunity in pediatric subjects, wherein said method comprises administersing an oral nutraceutical composition comprising prebiotic component and the beta-glucan in the ratio of 40:0.75 to 30:1.5.

[00157] In an embodiment, the application relates to method of improving the immunity in pediatric subjects, wherein said method comprises administersing an oral nutraceutical composition comprising prebiotic component and the beta-glucan, wherein the said composition further comprises one or more minerals selected from iron, zinc and selenium in an amount from 0.15 %w/w to 2.5 %w/w of the total composition.

[00158] In an embodiment, the application relates to method of improving the immunity in pediatric subjects, wherein said method comprises administersing an oral nutraceutical composition comprising a prebiotic component in an amount from 20% w/w to 40% w/w; and beta-glucan in an amount from 0.5% w/w to 5% w/w of the total composition, and wherein the said composition modulates the levels of immunity markers in the biological fluids of the subject by atleast 5% to 25%, when compared to the baseline levels of the immunity markers.

[00159] In an embodiment, the immunity markers can include, but are not limited to one or more of the Natural Killer cell (NK cell) activity, Immunoglobulin (IgA, IgE), Absolute Neutrophil Count (ANC), C-Reactive Protein (CRP) and combination thereof as measured thorough blood sample analysis.

[00160] In an embodiment, the immunity markers are assessed during and at the end of 1 month, 2 months, 3 months, 4 months, 5 months, 6 months, 7 months, 8 months, 9 months, 12 months and 24 months period.

[00161] In another embodiment, the application relates to a method of improving the immunity in pediatric subjects, wherein the said method comprises administersing an oral nutraceutical composition comprising a prebiotic component in an amount from 20% w/w

to 40% w/w; and beta-glucan in an amount from 0.5% w/w to 5% w/w of the total composition, and wherein the said composition increases the levels of immunoglobulins in the biological samples by atleast 5% to 25% when compared to the baseline levels.

[00162] In another embodiment, the application relates to a method improving the immunity in pediatric subjects, wherein the said method comprises administersing an oral nutraceutical composition comprising a prebiotic component in an amount from 20% w/w to 40% w/w; and beta-glucan in an amount from 0.5% w/w to 5% w/w of the total composition, and wherein the said composition increases the heamoglobin levels in the subject by atleast 5% to 20% when compared to the baseline levels.

[00163] In another embodiment, the application relates to a method improving the immunity in pediatric subjects, wherein the said method comprises administersing an oral nutraceutical composition comprising a prebiotic component in an amount from 20% w/w to 40% w/w; and beta-glucan in an amount from 0.5% w/w to 5% w/w of the total composition, and wherein the said composition when administered for a period of 1 to 3 months, shows an average of 86% reduction in respiratory illness, average of 95% reduction in incidence of cold, runny nose, and other respiratory issues from the baseline levels.

[00164] An embodiment of the application relates to the process of preparation of the nutritional composition.

[00165] In an embodiment, the application relates to the process for preparation of the nutritional composition comprising of a beta-glucan, prebiotic component and sugar base.

[00166] In an embodiment, the application relates to the process for preparation of the nutritional composition comprising of a beta-glucan, prebiotic component, a micronutrient component which comprises of one or more vitamins, minerals in a sugar base.

[00167] Another embodiment of the invention provides a process of preparing an oral nutraceutical composition, the said process comprising mixing the following ingredients:

a. a prebiotic component;
b. a beta glucan;
c. a micronutrient component comprising vitamins and minerals; and

d. one or more nutraceutically acceptable excipients.

[00168] In an embodiment, the invention relates to a process wherein the said prebiotic component is selected from fructans, Fructo-oligosaccharides (FOS), galacto-oligosaccharides (GOS), trans-galacto-oligosaccharides (TOS), starch, glucose-derived oligosaccharides, pectic-oligosaccharides, cocoa-derived flavonol or mixtures thereof.

[00169] In an embodiment, the invention relates to a process wherein the said beta-glucan is obtained from natural sources selected from barley, oats, rye, wheat, yeast or mixtures thereof.

[00170] In an embodiment, the invention relates to a process wherein the said beta-glucan is Wellmune obtained from yeast source.

[00171] In an embodiment, the invention relates to a process wherein the prebiotic component in an amount from 20% w/w to 40% w/w; and beta-glucan in an amount from 0.5% w/w to 5% w/w of the total composition.

[00172] In an embodiment, the invention relates to a process wherein the prebiotic component and the beta-glucan in the ratio of 40:0.75 to 30:1.5.

[00173] In an embodiment, the invention relates to a process wherein the said micronutrient component comprises one or more vitamins selected from Vitamin A, Vitamin B1, Vitamin B2, Vitamin B3, Vitamin B5, Vitamin B6, Vitamin B7 Vitamin B9, and Vitamin B12, Vitamin C, Vitamin D, Vitamin E, Vitamin K; one or more minerals selected from boron, calcium, chromium, copper, iodine, iron, magnesium, manganese, molybdenum, nickel, phosphorus, potassium, selenium, silicon, tin, vanadium, zinc or mixtures thereof.

[00174] In an embodiment, the invention relates to a process wherein the said micronutrient component comprises one or more vitamins selected from Vitamin A, Vitamin B6, Vitamin B9, and Vitamin B12, Vitamin C, Vitamin D, Vitamin E; one or more minerals selected from magnesium, iron, Zinc, selenium or mixtures thereof.

[00175] In an embodiment, the invention relates to a process wherein the micronutrient in an amount from 0.5 % to 8 % w/w of the total composition.

[00176] In an embodiment, the invention relates to a process wherein the said micronutrient component comprises the one or more minerals selected from iron, zinc and selenium in an amount from 0.15 %w/w to 2.5 %w/w of the total composition.

[00177] In an embodiment, the invention relates to a process wherein the said composition provides an energy density from 2 kcal/g to 10 kcal/g of the composition.

[00178] In an embodiment, the invention relates to a process wherein the process includes further mixing one or more gelling agents selected from gelatin, casein, collagen, guar gum, acacia, tragacanth, bug bean gum, pectin, starch, xanthan gum, dextran, succino glucan, carboxymethyl cellulose, ethyl cellulose, hydroxyethyl cellulose, hydroxypropyl cellulose, methylcellulose, sodium alginate or mixtures thereof.

[00179] An embodiment further relates to a process of preparation of the nutritional composition comprising:

a) beta-glucan, sugar base and a prebiotic
b) a micronutrient component essentially comprising of selenium, vitamin premix and mineral premix;
c) nutraceutically acceptable excipients

[00180] In an aspect of the above embodiments, the application further relates to a process of preparation of the oral nutritional composition preferably gummies.

[00181] According to one or more embodiments herein, the gummies prepared by the process known in the art including the teachings of the present application can be used in various products/ preparations including, but are not limited to candies, fitness supplements, vitamin / mineral formulas/multivitamin preparations, smoothies, fruit juices, powdered drinks, breakfast cereals, cereal bars, ice creams yogurts, dairy products, etc.

[00182] In an embodiment of the present application, the gummies prepared can be further subjected to tests of friability, disintegration and dissolution in order to ensure their bioavailability and modifications can be made to the compositions and process to comply with the necessary pharmacokinetic parameters by the person skilled in the art.

[00183] In another embodiment, the gummies of the present application are stable for the period of 9 months, when subjected to stability testing under 25 ℃/60% RH.

[00184] In another embodiment, the gummies of the present application are stable for the period of 9 months, when subjected to stability testing under 30 ℃/65% RH.

[00185] In another embodiment, the gummies of the present application are stable for the period of 9 months, when subjected to stability testing under 40 ℃/75% RH.

[00186] In another embodiment, the gummies of the present application are stable for the period of 12 months, when subjected to stability testing under 25 ℃/60% RH.

[00187] In another embodiment, the gummies of the present application are stable for the period of 12 months, when subjected to stability testing under 30 ℃/65% RH.

[00188] In another embodiment, the gummies of the present application are stable for the period of 12 months, when subjected to stability testing under 40 ℃/75% RH.

[00189] In another embodiment, the gummies of the present application are stable for the period of 24 months, when subjected to stability testing under 25 ℃/60% RH.

[00190] In another embodiment, the gummies of the present application are stable for the period of 24 months, when subjected to stability testing under 30 ℃/65% RH.

[00191] In another embodiment, the gummies of the present application are stable for the period of 24 months, when subjected to stability testing under 40 ℃/75% RH.

[00192] The present application is further illustrated by the examples provided merely to be exemplary of the pharmaceutical composition described above and do not limit the scope of the application. Certain modifications and equivalents will be apparent to those skilled in the art and are intended to be included within the scope of the present application.

[00193] The present invention is illustrated below by reference to the following examples. However, the one skilled in the art will appreciate that the specific methods and

results discussed are merely illustrative of the present invention and not to be construed as limiting the application. The following examples may include compilations of data that are representative of data gathered at various times during development and experimentation related to the present invention.

[00194] **Examples 1-7:** Oral chewable compositions of the present application

[00195] The compositions were prepared as given in Table 1

[00196] **TABLE 1**

Sr No.	**Raw material**	**Composition (% w/w)**						
		Example 1	**Example 2**	**Example 3**	**Example 4**	**Example 5**	**Example 6**	**Example 7**
1	Vitamin Premix	0.25	0.5	0.75	1.0	0.75	1.25	1.5
2	Mineral Premix	1.5	1.25	0.75	1.0	0.75	0.5	0.25
3	Pectin	2.50	2.50	2.50	2.50	2.50	2.50	2.50
4	Tri sodium citrate	0.45	0.45	0.45	0.45	0.45	0.45	0.45
5	Sugar(Sucrose)	35.00	34.75	34.5	34.25	34.5	34	33.75
6	FOS liquid	33.25	33.5	34.00	33.75	34.00	34.25	34.5
7	Citric acid monohydrate	1.30	1.30	1.30	1.30	1.30	1.30	1.30
8	Beta-glucan	1.00	1.00	1.00	1.00	1.00	1.00	1.00
9	Flavour	0.36	0.36	0.36	0.36	0.36	0.36	0.36
11	Colour	0.004	0.104	0.104	0.104	0.004	0.104	0.004

[00197] Manufacturing Process for gummies composition:

The process comprises of following steps:

Step I: Preparation of Sugar Syrup:

1. Sugar syrup is prepared by heating the mixture of desired quantity of sugar and appropriate quantity of water at predetermined temperature
2. FOS liquid is added to sugar syrup to obtain a homogenized solution.

Step II: Preparation of Micronutrient component:

Desired quantities of required vitamins and minerals are weighed and mixed to obtain vitamin premix and mineral premix respectively.

Step III: Desired quantities of all the excipients are measured.

Step IV: Preparation of final product (gummies):

1. Desired quantity of pectin is mixed with appropriate quantity of water and heated at predetermined temperature to obtain pectin syrup.
2. Pectin syrup and sugar syrup are mixed at predetermined temperature to get a homogenous bulk solution.
3. A slurry of beta-glucan powder and other dry ingredients including vitamin premix and mineral premix is made with water.
4. Homogenous bulk solution mentioned in Step IV (2) and slurry of ingredients mentioned in Step IV(3) are mixed together at a predetermined temperature.
5. Flavour is dispensed just before addition in to the batch.
6. The cooked bulk solution is transferred to deposition unit for deposition of gummies.
7. After deposition, gummies are collected and transferred to curing room for curing.
8. After curing gummies are subjected to sugar coating.
9. Throughout the entire process, optimized parameters like RPM for stirring, temperature, humidity etc. are maintained to ensure the proper formation of end product with desired properties.

[00198] **EXPERIMENTAL DATA**

Organoleptic Evaluation

Example 3 and Example 5 were subjected to physicochemical tests such as appearance, aroma, texture, taste, flavor etc.

Results of the tests are as follows:

I. <u>Organoleptic Evaluation:</u>

Examples 3 and 5 were subjected to organoleptic evaluation. Results of the evaluation are as mentioned below.

TABLE 2 : Organoleptic Evaluation

Test	Example 3	Example 5
Appearance	Dark amber coloured	Dark strawberry red
Aroma	Sweet aroma	Sweet aroma
Texture	Moderate Soft	Moderate soft and chewy
Flavour	Mango pulpy flavour	Pink guava flavour
Taste	Sweet and sour	Sweet and sour
After taste	Sweet and sour	Sweet and sour

II. Stability Study Data:

Examples 3 and 5 were subjected to stability testing under 40°C/75% RH conditions. The compositions were evaluated for their physicochemical properties, quantities of ingredients sustained in the compositions for different intervals of time and microbiological evaluation. Results of the stability tests are as mentioned below.

TABLE 3a: Physicochemical Evaluation of Example 3

Test	Unit	Specification	Example 3		
			0 month	3 Month	6 Month
Average gummy weight	g	2.97-3.63	3.2554	3.18	3.22
pH (5% Solution) at 25°C	-	3.0-4.5	3.51	3.5	3.5
Moisture Content (Vacuum Oven)	g/100g	NMT 12.0	9.14	9.0	9.2
Total Ash	g/100g	NMT 6.0	0.63	0.7	0.7

TABLE 3b: Physicochemical Evaluation of Example 5

Test	Unit	Specification	Example 5		
			0 month	3 Month	6 Month
Average gummy weight	g	2.97-3.63	3.17	3.19	3.19
pH (5% Solution) at 25°C	-	3.0-4.5	3.4	3.5	3.5
Moisture Content (Vacuum Oven)	g/100g	NMT 12.0	9.2	9.1	9
Total Ash	g/100g	NMT 6.0	0.8	0.7	0.7

TABLE 4a: Stability results for Example 3

The composition of Example 3 was analyzed for stability of major components/ ingredients at different intervals of time. The composition of Ex 3 showed excellent stability in terms of retention of the composition, wherein the major components of protein, carbohydrates, sugars, beta-glucan and FOS are retained within required label claim limits during and at the end of 6 month testing.

Test	**Unit**	**LC (Label Claim)**	**Specification**	**Example 3**					
				0 Time	%LC	3 Month	%LC	6 Month	%LC
Total protein	g/100g	2.5	2.25-2.75	2.52	101	2.45	98	2.49	100
Total carbohydrate	g/100g	86	77.4-94.6	87.71	102	88.2	103	87.7	102
Total sugars as sucrose	g/100g	34	31.1-37.95	34.28	101	34.85	103	34.63	102
Total calories	Kcal/100g	354	319-389	360.92	102	363	103	361	102
Beta-glucan	mg/100g	1000	900-1100	1052.1	105	1055	106	1052.5	105
FOS	g/100g	34	30.6-37.4	34.07	100	31.4	92	30.9	91

TABLE 4b: Stability results for Example 5

The composition of Example 5 was analyzed for stability of major components/ ingredients at different intervals of time. The composition of Ex 5 showed excellent stability in terms of retention of the composition, wherein the major components of protein, carbohydrates, sugars, beta-glucan and FOS are retained within required label claim limits during and at the end of 6 month testing.

Test	**Unit**	**LC (Label Claim)**	**Specification**	**Example 5**					
				0 Time	%LC	3rd Month	%LC	6th Month	%LC
Total protein	g/100g	2.5	2.25-2.75	2.45	98	2.46	98	2.44	98
Total carbohydrate	g/100g	86	77.4-94.6	87.6	102	87.8	102	87.9	102

Total sugars as sucrose	g/100g	34	31.1-37.95	34.58	102	35.6	105	34.67	102
Total calories	Kcal/100g	354	319-389	360	102	361	102	361	102
Beta-glucan	mg/100g	1000	900-1100	1058.2	106	1079.8	108	1094.5	109
FOS	g/100g	34	30.6-37.4	34.15	100	33.4	98	32.4	95

TABLE 5: Microbiological Evaluation of Example 3 and Example 5:

The microbiological evaluation of the compositions of Ex 3 and Ex 5, revealed no microbial growth during and at the end of 6 month testing period.

Test	**Unit**	**Specification**	**Example 3**	**Example 5**
			6 Months	**6 Months**
E.coli	cfu/g	Absent	Absent	Absent
Salmonella	cfu/25g	Absent	Absent	Absent
Total plate count	cfu/g	NMT 1000	<10	<10
Yeast and Moulds count	cfu/g	NMT 100	<10	<10

[00199] **Example 8: Clinical study**

[00200] An open label, interventional, single arm, study with children aged ≥3 to ≤7.0 years (N= 40 +- 10%) with hemoglobin level of ≥ 9 - ≤11 g/dl was conducted to assess the clinical impact of test compositions (Example 3 and Example 5). The study aimed to evaluate the effect of these oral compositions on immunity, bowel health and iron levels in children.

[00201] **The clinical study particularly evaluated:**

[00202] 1. The impact of the test compositions the on immunity in children using immunity markers and on Quality of life in children using the Quality-of-Life Questionnaire. The following Immunity Markers were assessed: Natural Killer cell (NK cell) activity, Immunoglobulin (IgA, IgE), Absolute Neutrophil Count (ANC), C-Reactive Protein (CRP) at baseline and 3 rd month.

[00203] The Quality of life was assessed through the KIDSCREEN QOL-27 Health Questionnaire for quality of life at Baseline, 1st month and 3rd month. Also, the blood iron levels were assessed at Baseline and 3rd month, through Hemogram test: Hemoglobin, RBC count, Total WBC and Differential WBC.

[00204] 2. The impact of the test compositions on immunity in children through the number of episodes of infection as recorded in the subject diary by parents or assigned caretakers. The data was captured for episodes of infection, type, number of episodes, frequency/severity, and duration of infection/allergies was captured as reported in subject dairy by parents/caregivers at Baseline, 1st month and 3rd month

[00205] **Study Treatment:**

Compositions of Example 3 and 5 as oral nutritional supplement.

Dosage Form: Gummies, 1 serve* of nutrition supplement in morning between the meals once daily. *(1 serve = 3 gummies).

[00206] **Results:**

[00207] The study results are as shown in the Table 6.

[00208] The study result show that > 90% of subjects showed an average of 12 % rise in haemoglobin levels from baseline ($p<0.001$).

[00209] The results have also shown significant improvement in immunity, observed through an average of 86 % reduction in respiratory illness, average of 95 % reduction in incidence of cold, runny nose, and other respiratory issues from the baseline at the end of 3 months of the study.

[00210] Also, highly statistically significant improvement is noted in addressing children's reluctance to pass stool (average 87% reduction in reluctance) subsequent to the introduction of the nutritional supplement.

TABLE 6

Parameter	**Baseline N=40 (mean +- SD)**	**3 month N=36 (mean +- SD)**	**% change from baseline (average) N=36**
Cd3 total cell counts (%)	62.2+-15.0	71.0+-10.0	10%
Immunoglobulin (IgA) g/L	1.30+-0.35	1.66+-0.32	17%
Immunoglobulin (IgE) IU/ml	360.6+-37.6	421.27+-41.7	13%
Haemoglobin g/dl	9.5+-0.5	11.8+-0.7	12%

WE CLAIM:

1. An oral nutraceutical composition comprising:
    a. a prebiotic component;
    b. a beta glucan;
    c. a micronutrient component comprising vitamins and minerals; and
    d. one or more nutraceutically acceptable excipients.

2. The composition as claimed in claim 1, wherein the said prebiotic component is selected from fructans, Fructo-oligosaccharides (FOS), galacto-oligosaccharides (GOS), trans-galacto-oligosaccharides (TOS), starch, glucose-derived oligosaccharides, pectic-oligosaccharides, cocoa-derived flavonol or mixtures thereof.

3. The composition as claimed in claim 1, wherein the said beta-glucan is obtained from natural sources selected from barley, oats, rye, wheat, yeast or mixtures thereof.

4. The composition as claimed in claim 3, wherein the said beta-glucan is Wellmune obtained from yeast source.

5. The composition as claimed claim 1, wherein the said composition comprises prebiotic component in an amount from 20% w/w to 40% w/w; and beta-glucan in an amount from 0.5% w/w to 5% w/w of the total composition.

6. The composition as claimed claim 1, wherein the said composition comprises prebiotic component and the beta-glucan in the ratio of 40:0.75 to 30:1.5.

7. The composition as claimed in claim 1, wherein the said micronutrient component comprises one or more vitamins selected from Vitamin A, Vitamin B1, Vitamin B2, Vitamin B3, Vitamin B5, Vitamin B6, Vitamin B7 Vitamin B9, and Vitamin B12, Vitamin C, Vitamin D, Vitamin E, Vitamin K; one or more minerals selected from boron, calcium, chromium, copper, iodine, iron, magnesium, manganese, molybdenum, nickel, phosphorus, potassium, selenium, silicon, tin, vanadium, zinc or mixtures thereof.

8. The composition as claimed in claim 1, wherein the said micronutrient component comprises one or more vitamins selected from Vitamin A, Vitamin B6, Vitamin B9, and Vitamin B12, Vitamin C, Vitamin D, Vitamin E; one or more minerals selected from magnesium, iron, Zinc, selenium or mixtures thereof.

9. The composition as claimed claim 1, wherein the said composition comprises micronutrient in an amount from 0.5 % to 8 % w/w of the total composition.

10. The composition as claimed claim 9, wherein the said micronutrient component comprises the one or more minerals selected from iron, zinc and selenium in an amount from 0.15 %w/w to 2.5 %w/w of the total composition.

11. The composition as claimed claim 1, wherein the said composition provides an energy density from 2 kcal/g to 10 kcal/g of the composition.

12. The composition as claimed claim 1, wherein the said composition further comprises one or more gelling agents selected from gelatin, casein, collagen, guar gum, acacia, tragacanth, bug bean gum, pectin, starch, xanthan gum, dextran, succino glucan, carboxymethyl cellulose, ethyl cellulose, hydroxyethyl cellulose, hydroxypropyl cellulose, methylcellulose, sodium alginate or mixtures thereof.

13. The composition as claimed in claim 1, wherein the nutraceutically acceptable excipients comprise of coloring agent, flavouring agent, acidity regulator and the like or mixtures thereof.

14. The composition as claimed in claim 1, wherein the composition is a tablet, capsule, granules, pellets, jelly, chewable tablets, gummies, lollipops, and other confectionary mimics.

15. The composition as claimed in claim 1, wherein said composition modulates the levels of immunity markers in the biological fluids of the subject by atleast 5% to 25% when compared to the baseline levels.

16. A method of improving the immunity in pediatric subjects, wherein the method comprises administersing an oral nutraceutical composition comprising:
a prebiotic component;
a beta glucan;
a micronutrient component comprising vitamins and minerals; and
one or more nutraceutically acceptable excipients.

17. The method as claimed claim 16, wherein the said composition comprises prebiotic component in an amount from 20% w/w to 40% w/w; and beta-glucan in an amount from 0.5% w/w to 5% w/w of the total composition.

18. The method as claimed claim 16, wherein the said composition comprises prebiotic component and the beta-glucan in the ratio of 40:0.75 to 30:1.5.

19. The method as claimed claim 16, wherein the said composition comprises one or more minerals selected from iron, zinc and selenium in an amount from 0.15 %w/w to 2.5 %w/w of the total composition.

20. The method as claimed claim 16, wherein the said method comprises administersing an oral nutraceutical composition comprising a prebiotic component in an amount from 20% w/w to 40% w/w; and beta-glucan in an amount from 0.5% w/w to 5% w/w of the total composition, and wherein the said composition modulates the levels of immunity markers in the biological fluids of the subject by atleast 5% to 25% when compared to the baseline levels.

21. The method as claimed claim 16, wherein the immunity markers is selected from one or more of the Natural Killer cell (NK cell) activity, Immunoglobulin (IgA, IgE), Absolute Neutrophil Count (ANC), C-Reactive Protein (CRP) and combination thereof.

22. The method as claimed claim 16, wherein the said method comprises administersing an oral nutraceutical composition comprising a prebiotic component in an amount from 20% w/w to 40% w/w; and beta-glucan in an amount from 0.5% w/w to 5% w/w of the total composition, and wherein the said composition increases the heamoglobin levels in the subject by atleast 5% to 20% when compared to the baseline levels.

23. A process of preparing an oral nutraceutical composition, the said process comprising mixing the following ingredients:

e. a prebiotic component;
f. a beta glucan;
g. a micronutrient component comprising vitamins and minerals; and
h. one or more nutraceutically acceptable excipients.

24. The process as claimed in claim 23, wherein the said prebiotic component is selected from fructans, Fructo-oligosaccharides (FOS), galacto-oligosaccharides (GOS), trans-galacto-oligosaccharides (TOS), starch, glucose-derived oligosaccharides, pectic-oligosaccharides, cocoa-derived flavonol or mixtures thereof.

25. The process as claimed in claim 23, wherein the said beta-glucan is obtained from natural sources selected from barley, oats, rye, wheat, yeast or mixtures thereof.

26. The process as claimed in claim 25, wherein the said beta-glucan is Wellmune obtained from yeast source.

27. The process as claimed in claim 23, wherein the prebiotic component in an amount from 20% w/w to 40% w/w; and beta-glucan in an amount from 0.5% w/w to 5% w/w of the total composition.

28. The process as claimed in claim 23, wherein the prebiotic component and the beta-glucan in the ratio of 40:0.75 to 30:1.5.

29. The process as claimed in claim 23, wherein the said micronutrient component comprises one or more vitamins selected from Vitamin A, Vitamin B1, Vitamin B2, Vitamin B3, Vitamin B5, Vitamin B6, Vitamin B7 Vitamin B9, and Vitamin B12, Vitamin C, Vitamin D, Vitamin E, Vitamin K; one or more minerals selected from boron, calcium, chromium, copper, iodine, iron, magnesium, manganese, molybdenum, nickel, phosphorus, potassium, selenium, silicon, tin, vanadium, zinc or mixtures thereof.

30. The process as claimed in claim 23, wherein the said micronutrient component comprises one or more vitamins selected from Vitamin A, Vitamin B6, Vitamin B9, and Vitamin B12, Vitamin C, Vitamin D, Vitamin E; one or more minerals selected from magnesium, iron, Zinc, selenium or mixtures thereof.

31. The process as claimed in claim 23, wherein the micronutrient in an amount from 0.5 % to 8 % w/w of the total composition.

32. The process as claimed in claim 31, wherein the said micronutrient component comprises the one or more minerals selected from iron, zinc and selenium in an amount from 0.15 %w/w to 2.5 %w/w of the total composition.

33. The process as claimed in claim 23, wherein the said composition provides an energy density from 2 kcal/g to 10 kcal/g of the composition.

34. The process as claimed in claim 23, wherein the process includes further mixing one or more gelling agents selected from gelatin, casein, collagen, guar gum, acacia, tragacanth, bug bean gum, pectin, starch, xanthan gum, dextran, succino glucan, carboxymethyl cellulose, ethyl cellulose, hydroxyethyl cellulose, hydroxypropyl cellulose, methylcellulose, sodium alginate or mixtures thereof.

35. The process as claimed in claim 23, wherein the nutraceutically acceptable excipients comprise of coloring agent, flavouring agent, acidity regulator and the like or mixtures thereof.

36. The process as claimed in claim 23, wherein the composition is a tablet, capsule, granules, pellets, jelly, chewable tablets, gummies, lollipops, and other confectionary mimics.

37. The process as claimed in claim 23, wherein said composition modulates the levels of immunity markers in the biological fluids of the subject by atleast 5% to 25% when compared to the baseline levels.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IN2024/050327

A. CLASSIFICATION OF SUBJECT MATTER

A61K31/00, A61K31/07, A61K31/702, A61K31/716, A61K33/00 Version=2024.01

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic database consulted during the international search (name of database and, where practicable, search terms used)

PatSeer, IPO Internal Database

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	IN202141021719A [PRAMANICK ANKUR, RAHEJA RONAK MANOJ KUMAR] 18-11-2022 (18 NOVEMBER 2022) refer abstract, claim 1-5	1-3, 7-8, 12-14, 23-25, 29-30 & 34-36
Y	Whole document	4-6, 9-11, 15, 26-28, 31-33 & 37
X	WO2020178720A1 [GLAXOSMITHKLINE BIOLOGICALS SA, WASHINGTON UNIVERSITY] 10-09-2020 (10 SEPTEMBER 2020) refer to the whole document	1-3, 7-8, 12-14, 23-25, 29-30 & 34-36
Y	Whole document	4-6, 9-11, 15, 26-28, 31-33 & 37
Y	WO2020252545A1 [FARMOQUIMICA SA] 24-12-2020 (24 DECEMBER 2020) refer abstract	1-15, 23-37

☐ Further documents are listed in the continuation of Box C. ☒ See patent family annex.

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"D" document cited by the applicant in the international application
"E" earlier application or patent but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
23-07-2024	23-07-2024
Name and mailing address of the ISA/ Indian Patent Office Plot No.32, Sector 14,Dwarka,New Delhi-110075 Facsimile No.	Authorized officer Akash Kumar Telephone No.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IN2024/050327

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 16-22
because they relate to subject matter not required to be searched by this Authority, namely:

see supplemental sheet

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/IN2024/050327

Citation	Pub.Date	Family	Pub.Date
WO 2020178720 A1	10-09-2020	EP 3930748 A1	05-01-2022
		US 20220168366 A1	02-06-2022
WO 2020252545 A1	24-12-2020	AR 116521 A1	19-05-2021
		BR 102019012637 A2	29-12-2020

International application No.
PCT/IN2024/050327

Continuation of Claims found unsearchable(Box II)

The subject matter of claims 16-22 relates to a method for treatment of the human by therapy (method of improving the immunity in pediatric subjects, wherein the method comprises administering an oral nutraceutical composition), which does not require an international search by the International Searching Authority in accordance with PCT Article 17(2)(a)(i) and [Rule 39.1(iv)].