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EFFECT OF PLANT LECTINS ON HUMAN BLOOD GROUP ANTIGENS WITH SPECIAL FOCUS ON PLANT FOODS AND JUICES

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ABSTRACT
Different plant lectins have been studied for lectin binding activity on ABO blood group system individually to study their suitability for consumption. 45% of plants were found to show blood group agglutination activity against A, B, AB and O groups. These results showed more suitability for consumption of investigated plants and their products to entire human population. Data also alarming human to be more careful about the plant lectins reacting with blood groups as the similar reactions may possibly happen at mucosal surface of the gut. In fact, chemical composition on RBC may similar with mucosal cell surfaces of human gastrointestinal tract. In our investigation results reveal that 27 percent of plant extracts showed activity against A, 38 percent of plant extracts for B, 45 percent plant extracts on AB and 45 percent of plants on O group blood populations of human beings. Further, O blood group humans have shown more significant activity (10 different plants) than A, B and AB. Hence, these double blind placebo studies are very promising and would give better results for suitability and digestibility of foods taking either as staple foods or juices, and also several health benefits for controlling the diet intake, based on the blood group type.
Keywords: Plant lectins, vegetable juices, blood groups, naturopathy

INTRODUCTION

Lectins are powerful tools for recognition of formidable range of oligosaccharides, which have been widely used in many branches of cell biology, biochemistry and food technology in applications. These are glycoprotein domains containing highly specific pockets for their counter sugar moieties of polysaccharides, glycolipids, glycoprotein's, proteoglycans and peptidoglycans present as outer surface markers or antigens on exterior walls or membranes of both vertebrate and invertebrate cells and micro-organisms. In fact, lectins participate in biological recognition phenomena in cell to cell contact of all living organisms involving cells and micro-organisms, for example binding of microorganisms to target tissues, sorting out proteins, control of morphogenesis, cellular differentiation, fertilization, adhesion and trafficking of leukocytes, metastasis, and inhibition of natural killer cell activity against healthy cells and so on[1-3]. By evolution, lectins have been performing variety of roles dealing with the defense mechanisms of plants. They protect plants against bacterial, fungal, and viral pathogens during seed imbibition, germination, and early growth of the seedlings[4]. Lectins have been identified to be detrimental to numerous insect and pests of crop plants. The majority of plant lectins are present in seeds, roots, stems and leaves. Most of them are best known components of human staple foods. Thus, lectin ingestion as part of any normal balanced diet is virtually unavoidable. One of the most nutritionally important features of plant lectins has high degree of resistance to gut proteolysis by the gastrointestinal tract of consumers. Some dietary lectins are poorly absorbed in the gastrointestinal tract and are relatively nontoxic at moderate concentrations[5]. This allows the lectins to bind to membrane glycosyl groups of the cells lining the digestive tract, which can be very well used as potential tools for specific drug targeting and bio-adhesive applications.

The human erythrocyte has 400 known blood group determinants that comprises of 15 genetically distinct blood group systems. However, ABO blood group and the Rhesus (Rh or D) blood group systems have major clinical importance. Depending upon the type of antigen on RBC, human population can be divided into four major groups A, B, AB and O and with Rh system (Antigen D) which could be either Rh factor positive or negative based on the presence of D- antigen on the red cells. ABO blood-group antigens are oligosaccharides exists as cell-surface glycoconjugates expressed by epithelia, endothelia and erythrocytes (RBCs) in primitive stage to humans[6]. These blood group antigens might have been evolutionarily advantageous in conferring resistance against pathogens and different foods[7]. The susceptibility to various diseases, such as infections, cancer, cardiovascular diseases and hematological disorders, has been associated with ABO blood groups[8]. During the evolution, humans migrated and were forced to adapt their diets to local conditions, the new diets provoked changes in their digestive tracts and immune systems, necessary for them to first survive and later thrive in their new habitats. Different vegetables metabolized in a unique manner by each ABO blood group containing individual blood group probably resulting in that blood group achieving a certain level of susceptibility (good or bad) to the viruses, bacteria, and parasites of the area. This was probably more than any other factor which has influenced the modern day distribution of our blood groups. It is fascinating to note that virtually all the major infectious diseases that ran so rampant throughout our pre-antibiotic history have ABO blood group preferences either one group or another. Blood group antigens such as glycoconjugates are found on the surface of cells lining

the digestive tract as well as on Red blood cells (RBCs). Almost every individual has antibodies to some dietary lectins in their bloodstream and many food allergies are due to the immune system reactions to these lectins[9]. The important point is that some of the lectins consumed in everyday foods act as chemical messengers that can in fact bind to the sugars of cells in the gut and the blood cells, initiating an inflammatory response[10]. Most dietary lectins will also stimulate polyamine production in the gut. Excess polyamine production released by lectins may be the result of an effort to repair the damage to intestinal microvilli caused by lectins. These lectins also are responsible for allergy in the gut causes release of IL-4, IL-13 and histamine which interfere with protein digestion and increase gut permeability[11-12].

The scientific study of current trends and the impact of medicinal and edible plants on animals including human, reveals that the people are attracting towards naturopathy for the past two decades for the treatment of many ailments being developed as a result of genetic disorders, environmental effects and various infections. Most of these complications are due to the sudden change of their lifestyles, increased global warming, tendency towards consumption of less processed foods, avoiding homemade foods, eating other unconventional mixed foods. Recently it has been observed that several raw plant products are being consumed as a part of naturopathy, in terms of juices either as mixed or combination of other food additives, other plant ingredients without concerning the tolerability, digestibility, palatability and other medical complications for curing several ailments (Table 1). Food intolerance is a clinical problem of digestive system against certain foods in human beings, restricted only when large amount of food taken. Food Allergy is an immune response to foods by vascular endothelial system (Gut) even at minor concentrations of allergic foods exists in the Gastro Intestinal Tract (GIT). In fact, it is very common in many individuals as everyone at one time or the other has a series of harmful local and systemic reactions triggered placing this class of molecules as anti-nutritive and/or toxic substances which had an unpleasant reaction to something they eat. Some people have specific food intolerances as well allergy against foods. Recent studies revealed that consumption of common food (individual specific), minor food with high biological activity; genetically modified (GM) foods may have major effects on the gut and body's metabolism. However, all these unfavorable conditions are not deliberately exploring. In author opinion it is due to the people (all classes) moving towards living in an environment where there is no time to see the kitchen and look after their buddies in the present scenario. Moreover, different unhealthy conditions making people to tempt to eat junk foods and non-conventional foods with high content of lectins not to suit their unique genetically operated food tolerance system of gut. Aero-digestive to uro-genital tracts cover with large lining of mucous membrane endowed with powerful mechanical and chemical cleansing mechanisms that degrade and repel most foreign matter. The anatomical components present in mucous membrane protect these surfaces against potential insults from the environment especially against colonization and invasion by potentially dangerous microbes, foreign proteinaceous lectins from ingested food. After ingestion, most dietary lectins bind to the absorptive microvilli of the small intestine. A study of extensive clinical and physiological data shows that the lectins – gut interactions vary from person to person and their internal and external effects are indeed augmentative at a statistically significant level. Locally, they can affect the turnover and loss of gut epithelial cells, damage the luminal membranes of the epithelium, interfere with nutrient digestion and absorption, stimulate shifts in the bacterial flora and modulate the immune state of the digestive tract. Systemically, they can disrupt lipid, carbohydrate and protein metabolism, promote enlargement and/or atrophy of key internal organs, tissues alter hormonal balance and immunological status. At high intakes, lectins can seriously threaten the growth and health of consuming individuals[13-15]. Therefore, lectins are powerful exogenous growth factors in the intestine, can alter the mucosal architecture, activity of endocrine cells and augment production of mucin in the small intestine while in the large intestine, they enhances selective over growth of microbial flora, increase M cells (playing major role in innate immunity) in the microvilla, and antigen independent lymphocyte proliferations as potent mitogens like PHA (Phytohemagglutinins from *Phaseolus vulgaris*) and ConA (Concanavalin – A from *Canavalia ensiformis*)[16-17]. In an experiment, comparative studies on effects of plant lectins on human gut indicated that there have also been ancient evolutionary effects shaping human body to be either tolerable or not to corresponding diet. In the gut, most of the digested food along with some lectins may gain access into the blood and lymph system through a process called endocytosis, which carries the intact lectin across the microvilli membranes as a vesicle[9]. Entered lectins through systemic circulation may travel towards liver, pancreas and systemic circulation where, depending on the lectin and person's unique glycoconjugates, it binds to glycosylated structures of other tissues of nervous and connective tissues. Plant lectins in the foods function as receptors to various cell surface glycoprotein's of gut, resulting in several important cellular mediated events, ranging from mitogenic processes to defense mechanisms[13,18-19]. They generally bind to insulin receptor, the epidermal growth factor receptor and the interleukin 2 receptor, which are very sensitive to the agglutinating effects of lectins. These cause several diseases including arthritis in human. In Rheumatoid arthritis, the basic difference between rheumatoid antibody (RA) and normal antibody is galactose, is replaced with N-acetyl glucosamine on RA might be the binding site for many plant lectins[20].

In oral mucosa, a close relationship is seen between the type of tissue differentiation and expression of blood group antigen; keratinized, non-keratinized, and junctional epithelium all show different patterns of carbohydrate expression[21]. These foods act as sacrificial decoys and attach to the problematic lectins that would ordinarily attach and bind to gut epithelial cells. A specific glycoprotein of animal body having N-acetyl glucosamine (NAG) is also a structural component of many microbes, a favourite target for dietary lectins and is

concentrated in connective tissue. Supplementation with NAG is an excellent strategy for lectin protection. Another sugar with similar activity is D-mannose, which is capable of binding to lectins located on the cells of microorganisms. Some bacteria responsible for urinary tract infections contain lectins specific for the sugar mannose and use these lectins to bind tightly to mannose-rich tissue in the bladder walls, initiating urinary tract infections[22]. As with Bladder wrack and NAG, supplementation with D-mannose provides a decoy for these lectins and protects the bladder. Supplementing prior to a meal with these decoy sugars allows for the binding of potentially harmful lectins and protection from attack. This concept of lectin-shielding devices has exciting clinical application now and in the future[23]. This might be the common practice in China to protect from many infections. There are even some lectins that are beneficial to the body, such as those found in some species of edible snails, which may be capable of preventing the metastasis of cancer cells[24].

The involvement of lectins in our health and their relationship to degenerative disease is still an emerging science. Studies performed on animals will continue to be the model in the future for the study of lectins. The glycosylation of the human gut is basically similar to that of higher animals and it may be confidently predicted that the effects of dietary lectins will have similarities in both humans and animals. In short, dietary lectins, by their chemical reactivity with cell surface receptors on the intestinal epithelium, are metabolic signals for the gut and are capable of modulating immune and hormone functions[9]. Most of the biomolecules along with microbes (Virus, bacteria, fungi etc) primarily bind (controlled good or bad) to the receptors and decide whether the molecule have to enter into the blood stream or not. This physiological phenomena has its great importance to understand the host- parasite; receptor-ligand interaction. In view of several binding abilities of lectins to diverse cell population, scientists have already started using them for blocking some infectious agents.

Invitro studies conducted on HIV showed that jacalin, a lectin is completely blocking HIV Type –I *in vitro* infection to lymphocyte. Main cause of AIDS is the formation of Syncytia by fusion of HIV infected cells with uninfected T cells results cellular disorganization and reducing of T_H Cell (<200 cell/dl blood) count[25]. Previous results also demonstrate that innate defense lectins can provide immunity against pathogens that display blood group self-antigens on their surface[26]. In fact similar antigenic (ABO) system does exist on surfaces of all endothelial and surface cells of human individuals. This lectin based interaction could decide whether particular plant food is tolerable; microorganism can exist at microbial flora at gut; any allergic receptors would develop or not. Keeping all these advantages in view, we have initiated to screen all edible and other related plant and its products being used as naturopathy for treating different ailments or staple food either in native form or mixed form for determining the edibility, selectivity and palatability to every individual based on their blood group. We are also hoping that lectins from several plants showing variation in agglutination of blood group systems useful for finding correct remedies in the pathogen mediated/, and lectin mediated syncytia formation, of-course this can only be revealed by animal studies. Thus, novel toxicological/nutritional methods are urgently needed to screen for harmful consequences of different intolerable, GM and allergic foods on human/animal health. This article further helps researchers who are working on the impact of lectins on human aero-digestive and uro-genital tract system to alleviate potential risks of these lectins when consumed at concentrations normally present in foods and the steps taken by regulators to mitigate exposure where possible.

MATERIALS AND METHODS

Blood collection from human subjects

Blood samples were taken from healthy males aged between 25 – 30 years (Average: 28.3, SD $\pm$ 1.5 years), without psychiatric, neurological or somatic disorders or a history of head injuries, lipid or carbohydrate metabolism disorders, with a normal body mass index, and not being treated with any drugs. Healthy subjects (no smokers) who do not use any addictive substances and antioxidant supplementation, and their diet were balanced (meat and vegetables). They lived in similar socioeconomic conditions. Psychiatric examination (using the M.I.N.I. – Mini International Neuropsychiatric Interview), and neurological and somatic examinations were performed[27]. Human blood (3 X 7.5 ml) was collected into ACD solution (Citric acid/Citrate/Dextrose; 5: 1 v/v) between 8.00 and 8.30 a.m. The blood was stored at 4ºC with the help of trained practitioner. Blood samples were collected under the supervision of Dr. G. Uma Ramani, Dept. of Biochemistry, ASRAM super specialty teaching hospital, Eluru, West Godavari Dist.,A.P., India, after obtaining the consent of the patients. The experiments were conducted according to the ethical guidelines suggested by the Institutional Animal Ethics committee for the purpose of Control and supervision of Experiments on Animals (CPCSEA), Ministry of Environment and Forest, Government of India.

ACD blood anticoagulant

1.32g of sodium citrate dissolved in 85ml of distilled water to which 0.48g of citric acid and 1.47g of dextrose are added. Total volume of this mixture has been made into 100ml with double distilled water and sterilized with 0.2µm membrane system.

Phosphate buffer

22.6 ml percent solution containing 14.1g of Na_2HPO_4 (w/v) mixed with 77.4 ml of percent solution containing 15.6 g of NaH_2PO_4 (w/v) and to which 0.8g of NaCl was added and pH adjusted to 7.4.

Plant material

Plant parts were collected from campus garden as well as outside the campus of K L University, Guntur district and at different parts of North Coastal AP during September 2009–February 2011. All the plants were identified and confirmed by the taxonomists of Andhra University, Visakhapatnam and a set of specimen were deposited at our University centre. The plant materials were thoroughly washed first with tap water and then rinsed with distilled water followed by double distilled water.

Crude extracts are prepared in phosphate buffered saline, PBS (pH 7.4) to get 20% (w/v) extract.

Preparation of extracts

Different plant parts, which are being used for screening and isolation of lectins, were collected from the available sources and taxonomically identified. Direct macerated/ crushed plant part extracts were prepared by mortar and pestle and squeezed, followed by centrifuged at 10,000 g for 10 minutes to get clear extract. Lowry et al., method[28] has adopted to quantify the resulted extracts in terms of protein concentration. The plant sources, which are not being used as juices, curries and are hard to extract were ground into powder and extracted into Phosphate buffered saline (pH 7.4). This mixture was transferred into a gauge cloth there by leaving the extract on the top and aqueous layer collected into centrifuge tubes. These tubes were then centrifuged at 10,000 rpm for 3-5 minutes. The supernatant was separated and stored. The blood samples from different blood groups A, B, AB and O were collected.

Heme agglutination assays

The blood samples from different individuals having blood groups A, B, AB and O were collected and stored in ACD solution. Assay of heme Agglutination carried out according to the Blackall et al method[29]. Care has been taken to avoid misinterpretation as a positive result by peripheral drying. Agglutination of red blood cells within two minutes indicates the presence of antigen on human red blood cells. Absence of agglutination indicates the absence of corresponding blood group antigens on the human red blood cells. A negative along with positive controls were made with 10% saline.

RESULTS AND DISCUSSION

80 different plants, which are being used by all classes of human population in regular life, were screened for identification of lectins against four individual blood group system (ABO) from corresponding plants and their edible/ usable part to study the selectivity as staple food to the corresponding human as blood type diet. All these plants/ plant parts are directly/ indirectly/ regularly/ occasionally used by animals including human beings as staple food, folklore medicine working as remedy under Nature therapy or Naturopathy. All these plants and their parts were selected as per the existing information and knowledge available with parents (Grandparents from both paternal and maternal), books, articles, folklore, data collected from tribal's and literature survey (Table 1).

It has been observed that only certain plant parts were recommended for daily use as ingredients of staple food, curries, pickle making etc., and some parts never recommend for any use due to the presence of lectins and toxins even in the modern medical system (Allopathy). Our earlier studies (unpublished data) reveal that they are very good sources for lectins. Because of these reasons forefathers and other knowledge sources might not recommend it to use these plant parts as food and folklore medicine. Our experimental results shows that 36 plants out of 80 plants and their different parts tested, found to contain lectins. Plants which show good agglutination activity against ABO blood group systems are further studied to their avidity or binding strength in turns of their titer (Table 2). A titer can be defined as the final concentration at which lectin still giving precipitation reaction with corresponding blood group. 96 extracts of 80 different plants which showed agglutination activity when further analyzed revealed that 27% of plant extracts have different levels of titers against blood group 'A', 38% of plant extracts against B, 45% for AB and 45% to O blood group. Even though all are showing different binding affinities, only 10 plants showed highest titer value i.e., 1024 against O and less titer in 6, 3, 1 plant(s) each against AB, B and A respectively. These reports are closely correlating with geographical existence of ABO blood groups.

In our experiments about 44 plants were not shown any lectin activities against any one of the blood groups tested. Authors opined that these plants have long standing relationship with human blood cells and during the evolution, body weight be slowly energized due to the above foods. Out of 44 plants, which showed no activity against any one of the blood groups are the regulator staple food of all classes of human irrespective of the geographical region, races or any other parameter that are currently using to classify the human population throughout the globe. Most of the plants investigated and their seeds, leaves, and other parts are being using as ingredients for making curries, pickles, main components of folklore homemade medicine, cocktail homeopathic drugs designed for oral routes only. Author assuming that, this report showing a direct significant correlation with no lectin activity in these plants against all blood groups tested and has great evolutionary significance in the diversified tolerance development to these foods in the internal lining of the gut from mouth to anus of the human being. Some of the lectins present in the staple foods are heat-stable and react with gastrointestinal tract causes subclinical effects in higher animals and humans, particularly when consumed in large quantities[30]. Dietary lectins in excess can cause the following physiological effects such as gastrointestinal damage, Type-2 IgG immune responses, anti-nutritional, mild allergic and heme agglutination. Lectins present in the vegetarian foods were inactivated by heating and moist heat was more active than dry heat. The results suggest that lectins may not be responsible for short term toxicity caused by consumption of raw meal[31]. Although lectin containing foods are frequently consumed cooked or otherwise processed, these treatments may not always inactivate the lectins, although some lectins are heat liable. However, some lectins can be removed from foods by different technological processes such as by soaking, autoclaving, and toasting processes. Even though all edible parts investigated are found to contain lectins, their activities in terms of binding affinity and agglutination ability towards all classes of blood groups i.e A, B. AB, O both Rh positive and Rh negative are entirely different. This great diversity among the plant lectins against blood group antigens and lectins were measured interns of their titer values. Where two or four fold diluted RBC are treated with lectins from plants. The final concentration of RBC (in terms of dilution factor) up to now still showing agglutination with RBC but next dilution may not be identified as titer (Table 2).

Table 1: Different fruit juices that are recommended by natural therapists against various ailments

S.N	Name of the plant	Vernacular name	Part used	Prophylactic activity (Naturopathy)
1.	*Allium sativum*	Garlic juice	Bulbs	Anti-diabetic, improve digestion, relieve cough, fever, paralysis, forgetfulness, tremor, colic pains, internal ulcers, and anti-inflammatory response, Rheumatism, intestinal worms, colic, flatulence, dysentery, liver disorder, tuberculosis, facial paralysis, high BP and bronchitis, eczema and scabies.
2.	*Ananas comosus (L.)* Merr.	Pineapple	Fruit	Anti-inflammatory, reduce swelling, acute sinus, sore throat, arthritis & gout, goiter, catarrh, high BP, remove intestinal worms and constipation.
3.	*Azadirachta indica*	Neem	Leaves	Anti-inflammatory, anti-arthritic, antipyretic, hypoglycemic, anti-gastric ulcer and spermicidal.
4.	*Benincasa hispida*	Watermelon /White guard/Ash guard	Fruit	Increase appetite, cure kidney stones. Increase sperm count and locomotion. Lowers fat in the body & urinary problems, avoid burning sensation, good for liver, high BP, diabetes and losing weight
5.	*Beta vulgaris*	Beetroot	Root	Anti-diabetic, weight loss, antitumor, anemia, hepatitis, jaundice, hypoglycemia, diarrhea, constipation, hemorrhoids, dysentery, hypertension, heart troubles, acidosis. Useful for boils, skin inflammation, pimples, pustules, measles and dandruff.
6.	*Carica papaya*	Papaya	Fruit	Avoid digestive disorders, ulcers, skin infections, warts and related skin tags, removes blood stains and fat stains
7.	*Citrullus lanatus*	Watermelon	Fruit	Anti-Aging, curing renal and bilious problems, risk of kidney stones, CVD, Anti-Cancer, decrease in ailments of prostate and oral cancers, allergy, Asthma, osteoarthritis, high BP, Anti-inflammatory, Anti-viral, Antioxidant and analgesic potential
8.	*Citrus fruits*	All varieties	Fruits	Prevent Scurvy, enhance digestion, cures constipation, Improves immune system and benefits to skin
9.	*Cucumis melo*	Muskmelon	Fruit	Beneficial to lack of appetite, weight loss, urinary tract infections constipation, acidity, ulcer, laxative and diuretic
10.	*Daucus carota*	Carrot	Root	Diuretic, remineralizing, anti-diarrheal, tonic and anti-anemic, maintain acid-alkaline balance of blood and body, prevent bleeding of gums, Anti-inflammatory, immune system tonic, effective against roundworms and dandruff. Tonsillitis, colitis, appendicitis, gravel acidosis, ulcers, rheumatism, adenoids and cancer.
11.	*Fragaria vesca*	Strawberry	Fruit	Improve urine flow, good remedy for chronic diarrhea, kidney diseases, intestinal worm, pulmonary inflammation, catarrh, gout, arthritis, jaundice, liver, stomach problems, bladder stones, indigestion and anemia,
12.	*Lagenaria siceraria*	Bottle guard	Fruit	Cooling, diuretic, sedative and anti-bilious, Urinary disorders, constipation, weight loss, diarrhea and diabetes
13.	*Malus domestica*	Apple	Fruit	Antioxidant, pro-inflammatory free radicals from the body; Lower cholesterol levels, antiviral, increase digestion, detoxification, source of fibre and anti-diarrhoea
14.	*Mangifera indica*	Mango	Fruit	Anti-oxidant, anti-inflammatory, anti-diarrhea, dysentery, analgesic, immunomodulatory; relieve from constipation, dermatological disorders, AIDS, Cancer and asthma. Increase hemoglobin in blood, aphrodisiac, rejuvenate male reproductive system and increase semen.
15.	*Momordica charantia*	Bitter guard	Fruit	Anti-diabetic, Antihelmintic, Antimalarial, antiviral, Cardio protective, anti-cancer, Dysentery, Scabies. Piles, Blood disorders, Respiratory disorders, Cholera and alcoholism.
16.	*Musa paradisiaca*	Banana	Fruit	Anaemia, BP, brain power, constipation, depression, hangovers, heartburn, morning sickness, mosquito bites, ulcer, warts, stress and strokes.
17.	*Pouteria sapota*	Sapota	Fruit	Hair tonic, dermatitis of the scalp and hypertension.
18.	*Psidium guajava*	Guava	Fruit	Anticancer, antidiarrheal, antimicrobial, antispasmodic, astringent. Lowers diabetes, dysentery and fever.
19.	*Punica granatum*	Pomegranate	Fruits	Anti-diabetic, weight loss, antimicrobial, antioxidant. Prevent heart diseases, total cholesterol, LDL, anti-cancer, CVD, Wound healing and immune boosting.
20.	*Solanum lycopersium*	Tomato	Fruit	Anticancer- breast, bladder, cervix, colon and rectum, stomach, lung, ovaries, pancreas, pancreas and prostate. Lowers diabetes, CVD, cataracts, asthma, high BP, osteoarthritis, common cold, chills and digestive disorders.
21.	*Trichosanthes cucumerina*	Snake guard	Fruit	Natural antibiotic, expectorant, laxative, disperse phlegm, remove pus, anti-inflammatory, tonic for heart, tuberculosis, Anti-diabetic, Jaundice, purgative, alopecia. Antitumor and management of AIDS.
22.	*Trigonella foenum-graecum*	Fenugreek	Leaves	Anti-diabetic, Reduce intestinal gas, avoid pain and bloating, diarrhea, throat pain, ulcers, open sores in and around the mouth, alleviate swelling and pain, Anemia, anti-inflammatory, antitumor, laxative and febrifuge.
23.	*Vitis vinifera*	Grapes	Fruit	Diziness, vertigo, headache, diarrhea, Wrinkles, pimples, stretch marks, conjunctivitis, Nosebleeds, antioxidant and fibromyalgia, dry skin, skin diseases – eczema, itching, skin spots.

CVD= Cardio vascular diseases

Table 2: Agglutination* titers of erythrocytes by crude lectins of different plants

S.NO	Plant name	Vernacular name	Family	Part used	Agglutination titer			
					A	B	AB	O
1.	*Annacardium occidentale*	Cashew	Anacardiaceae	Leaf	8	8	8	64
				Fruit	64	32	8	256
2.	*Averrhoa carambola*	Carambola/ Star fruit	Oxalidaceae	Fruit	32	32	64	64
3.	*Azadirachta indica*	Neem	Meliaceae	Leaf	–	–	–	64
4.	*Benincasa hispida*	Winter melon/ Ash gourd	Cucurbitaceae	Seed	128	8	64	128
				Flesh	–	–	–	–
5.	*Calotropis gigantea*	Crown flower	Apocynaceae	Seed	64	8	64	64
6.	*Carica papaya*	Papaya	Caricaceae	Fruit	256	256	8	1024
				Seeds	–	–	–	–
7.	*Cucumis melo*	Muskmelon	Cucurbitaceae	Fruit	8	128	8	16
8.	*Cucumis sativus*	Cucumber	Cucurbitaceae	Seed	16	–	–	16
				Flesh	–	–	64	256
9.	*Dodonaea angustifolia*	Sand olive	Sapindaceae	Seed	–	–	32	–
				Flower	–	–	–	–
10.	*Emblica officinalis*	Amla/ Indian gooseberry	Phyllanthaceae	Seed	–	8	–	16
				Fruit	–	–	–	–
				Leaf	–	64	16	32
11.	*Fragaria ananassa*	Strawberry	Rosaceae	Fruit	8	8	8	64
12.	*Hibiscus esculatum*	Okra, lady's fingers	Malvaceae	Leaf	–	64	4	64
				Fruit	–	16	8	16
				Seed	–	8	8	–
13.	*Jatropha curcas*	Barbados Nut/Purging Nut	Euphorbiaceae	Leaf	64	64	32	64
14.	*Lagenaria siceraria*	Bitter gourd	*Cucurbitaceae*	Fruit	–	–	–	64
				Leaf & Seeds	–	–	–	–
15.	*Luffa acutangula*	Ridged luffa	Cucurbitaceae	Seed	–	–	64	8
16.	*Malus domestica*	Apple	Rosaceae	Fruit	–	–	64	–
17.	*Mangifera indica*	Mango	Anacardiaceae	Leaf	–	–	128	–
				Fruit	–	8	–	16
18.	*Mimosa pudica*	Touch-me-not	Fabaceae	Leaf	8	32	–	32
19.	*Momordica charantia*	Bitter guard	Cucurbitaceae	Seed	16	64	8	32
				Fruit	–	512	512	256
				Leaf	–	16	–	–
20.	*Ocimum sanctum*	Wild Tulasi	Labiatae	Leaf	–	–	–	64
21.	*Phaseolus vulgaris*	Black kidney bean	Fabaceae	Seed	32	64	512	512
				Rind	8	–	–	–
22.	*Phyllanthus acidus*	Otaheite gooseberry	Phyllanthaceae	Leaf	–	32	32	–
				Seed	–	–	–	–
				Fruit	–	–	–	–
23.	*Phyllanthus niruri*	Stonebreaker	Phyllanthaceae	Leaves	8	16	8	64
				Root	–	4	4	4
24.	*Pouteria sapota*	Sapota	Sapotaceae	Fruit	256	1024	1024	1024
25.	*Ricinus communis*	Caster	Euphorbiaceae	Fruit	1024	1024	1024	1024
26.	*Rubia cordifolia*	Common Madder	Rubiaceae	Leaf	–	32	–	–
27.	*Solanum melongena*	Brinjal	Solanaceae	Seed	64	8	64	32
				Fruit	8	16	32	32
28.	*Thevetia peruviana*	Yellow Oleander	Apocynaceae	Leaf	–	–	8	128
29.	*Tridax procumbans*	Coat buttons/ tridax daisy	Asteraceae	Whole plant	–	–	16	–
				Flower	–	–	16	16
				Leaf	16	16	8	8
30.	*Vitis labrusca*	Black Grapes	Vitaceae	Fruit (UR)	512	512	64	4
				Peel	–	–	32	32
				Flesh	32	1024	1024	1024
				Seed	–	8	256	–
31.	*Vitis vinifer*	Green grapes	Vitaceae	Fruit (UR)	–	–	512	64
				Peel	–	–	–	–
				Flesh	256	256	1024	1024
				Seed	–	–	–	–
32.	*Raphanus sativus*	Radish	Brassicaceae	Tuber	32	8	8	16
33.	*Tamarindus indica*	Indian date	Caesalpiniaceae	Young leaf	–	32	32	8
34.	*Piper betle*	Betel	Piperaceae	Leaf	32	8	512	256
35.	*Camellia sinensis*	Tea	Theaceae	Young Leaf	8	8	64	64
36.	*Amaranthus oleraceus*	Amaranthus	Amaranthaceae	Leaf	–	–	64	64
37.	*Abelmoschus esculentus*	Ladyfinger	Malvaceae	Seed	–	–	–	–
				Fruit	–	–	–	–
38.	*Allium sativum*	Garlic juice	Liliaceae	Bulb	–	–	–	–
39.	*Aloe barbadensis*	Aloe vera	Xanthorrhoeaceae	Leaf	–	–	–	–
40.	*Alternanthera triandra*	Matsyakshi	Amaranthaceae	Leaf	–	–	–	–
41.	*Amaranthus caudatus*	love-lies-bleeding	Amaranthaceae	Seed	–	–	–	–
42.	*Amaranthus mangostanus*	Amaranth	Amaranthaceae	Seed & Leaf	–	–	–	–
43.	*Ananas comosus (L.)*	Pineapple	Bromeliaceae	Fruit	–	–	–	–

44.	*Basella alba*	Phooi leaf	Basellaceae	Leaf	–	–	–	–
45.	*Beta vulgaris*	Beet	Amaranthaceae	Root	–	–	–	–
46.	*Boswellia serrata*	Indian frankincense	Burseraceae	Powder	–	–	–	–
47.	*Brassica nigra*	Black mustard	Brassicaceae	Seed	–	–	–	–
48.	*Calotropis procera*	Apple of Sodom	Asclepiadaceae	Fruit	–	–	–	–
49.	*Catharanthus roseus*	Madagascar periwinkle	Apocynaceae	Leaf & Flower	–	–	–	–
50.	*Centella asiatica*	Centella	Mackinlayaceae	Leaf	–	–	–	–
51.	*Chrysanthemum cinerariaefolium*	Mums/ chrysanths	Asteraceae	Leaf & Flower	–	–	–	–
52.	*Cissus quadrangularis*	Veldt Grape/ Devil's Backbone.	Vitaceae	Stem Powder	–	–	–	–
53.	*Citrullus lanatus*	Watermelon	Cucurbitaceae	Pulp & Seeds	–	–	–	–
54.	*Coffea arabica*	Coffee shrub of Arabia	Rubiaceae	Seed	–	–	–	–
55.	*Coriandrum sativum*	Coriander	Apiaceae	Seed & Leaf	–	–	–	–
56.	*Cucumis sativus*	Cucumber	Cucurbitaceae	Fruit & Seed	–	–	–	–
57.	*Eclipta alba*	False Daisy/ bhringraj	Asteraceae	Leaf	–	–	–	–
58.	*Hibiscus cannabinus*	kenaf	Malvaceae	Leaf & Flower	–	–	–	–
59.	*Hibiscus rosasinensis*	China rose	Malvaceae	Leaf	–	–	–	–
60.	*Holarrhena antidysenterica*	Bitter Oleander	Apocynaceae	Leaf	–	–	–	–
61.	*Mentha viridis*	Mint	Lamiaceae	Leaf	–	–	–	–
62.	*Moringa oleifera*	Drumsticks	Moringaceae	Fruit	–	–	–	–
63.	*Musa paradisiaca*	Banana	Musaceae	Fruit	–	–	–	–
64.	*Ocimum sanctum*	Holy Basil	Lamiaceae	Powder	–	–	–	–
65.	*Ocimum tenuiflorum*	Tulasi (Small)	Labiatae	Leaf	–	–	–	–
66.	*Piper betle*	Betel	Piperaceae	Leaf	–	–	–	–
67.	*Piper nigrum*	Black pepper	Piperaceae	Seed	–	–	–	–
68.	*Pisum sativum var. macrocarpon.*	Green pea	Fabaciae	Whole fruit	–	–	–	–
69.	*Plumeria rubra*	Temple Tree	Apocynaceae	Bark	–	–	–	–
70.	*Prunus amygdalus*	Almond	Rosaceae	Seed	–	–	–	–
71.	*Psidium guajava*	Guava	Myrtaceae	Fruit	–	–	–	–
72.	*Punica granatum*	Pomegranate	Lythraceae	Pulp & Seeds				
73.	*Samanea saman*	Rain tree	Fabaceae	Leaf	–	–	–	–
74.	*Solanum lycopersium*	Tomato	Solanaceae	Pulp & Seeds	–	–	–	–
75.	*Spinacia oleracea*	Spinach	Amaranthaceae	Seed	–	–	–	–
76.	*Strychnos nux vomica*	Poison Nut	Loganiaceae	Root	–	–	–	–
77.	*Symplocos racemosa*	Symplocos Bark	Symplocaceae	Powder	–	–	–	–
78.	*Tagetes patula*	French mary gold	Asteraceae	Leaf	–	–	–	–
79.	*Trichosanthes cucumerina*	Snake gourd	Cucurbitaceae	Fruit	–	–	–	–
80.	*Trigonella foenum-graecum*	Fenugreek	Fabaceae	Whole plant	–	–	–	–

* Highest dilution of crude lectin preparation causing detectable agglutination after 1 hour at room temperature.
UR= Un-ripened; RD=Ripened; – = Appropriate agglutination not observed.

Earlier studies describes that the potential actions of food lectins are not at all bad. They have been identified to manage different ailments to control at optimum level such as (i) Direct insulin-mimetic and insulin sparing properties, (ii) Serving a structural role as anchoring molecule, (iii) Serving an anti-parasitic function in plants against their pathogens, (iv) Involved in the wound sealing mechanism by secreting proteins analogue to blood clotting proteins in vertebrates, (v) Subsequent to wound-sealing the lectin by virtue of its being there might protect against any further infection, (vi) Molecule responsible for acting as anti-microbial, anti-protozoal and anti-cancer, (vii) Lowering effects against obesity, hypercholesterolemia, high blood pressure, cardiovascular diseases, neural disorders etc (viii) Using as cosmetics. Therefore, lectins of plant origin playing a crucial role in the daily life of all living organisms based on their geographical existence, genetic constitution and adaptability to the concerned plant products/ food from early growth stage of the human beings[32-33].

Screening, identification and recognition of self components to ensure tolerance, to environmental components, to communicable bacteria, to foods that are consuming either as food ingredients or medicine is under the control of gut immune system associated with gastrointestinal surface area extending from mouth to anus where RBC antigens present on lining of gut playing an initiator role. This is a highly complex process consists of recognition, response, elimination and memory and ultimately develops tolerance. The development of tolerance is the result of active immune mechanisms and both development and maintenance of tolerance are lifelong processes which start very early in life, even prenatally. Exposure to bacteria during birth and from the mother's skin and the provision of immunologic factors in breast milk are amongst the key events that promote maturation of the infant's gut and gut-associated and systemic immune systems. The introduction of formula and of solid foods exposes the infant to novel food antigens and also affects the gut flora[34]. Nutrition may be the source of antigens to which the immune system must become tolerant, provide factors, including nutrients; they themselves might modulate immune maturation and responses, and provide factors that influence intestinal

flora, which in turn will affect antigen exposure, immune maturation and immune responses. Through these mechanisms it is possible that nutrition early in life might affect later immune competence and surveillance, such as the ability to mount an appropriate immune response upon infection, the ability to develop a tolerogenic response to 'self' and to benign environmental antigens, and the development of immunologic disorders[35]. In recent years, however, due to the negative effects of technological development upon various social and environmental processes, the relationship between human beings and nature has received more and more recognition. According to the American Cancer Society, "Available scientific evidence does not support claims that naturopathic medicine (is a philosophy-based, whole medical system) can cure cancer or any other disease, since virtually no studies on naturopathy as a whole have been published".

In earlier studies one of the authors reported that the allergic proteins present in the staple foods may contain components to induce either food intolerance or food allergy[17, 36]. These interactions are result of binding of either surface lectins of GIT or lectins of foods with counter sugar molecules present in the foods or anchored sugar moieties on the GIT respectively. Investigations on food lectins interaction with gut reveal that there is a direct correlation between evolution of blood groups and types of food intake[37]. Development of blood groups based on many factors like genetic constitution, geographical and environmental factors adaptation to type of food from early days of growth during the evolution. Anthropologists recommended the order of blood groups development based on their food habits[38-41]. This concept states that the first blood group evolved on earth is 'O' belongs to ancient hunter-gatherers and ate a diet dominated by meat and developed antibodies against the lectins found in agricultural foods. The next blood type to evolve was type A are pure vegetarians, these people began to grow food rather than hunt it as a result of change of environmental conditions. In between next blood type to emerge was type B as a consequence of ancient people migration and further climate change. These people habituated to the diet included meat and plants as well as dairy products. The final blood type to evolve was type AB. It is a rare blood type even today with fewer than 4% of the world's population and evolved when the A and B blood types intermingled[42-43]. This report is directly correlating with present existence of different blood groups of human population as O (44%), A (42%), B (10%) and AB (4%) and also the results observed in our investigations. Naturo-therapists suggest several plants products to be taken as raw juices such as Ashgaurd juice for improvement of sperm count; Watermelon, Bitter guard and strawberry juices for avoiding aging affects; Bottle guard for weight loss; Fenugreek, Garlic, Pomegranate juice for lowering the diabetes etc. However, there are no FDA regulations or guidelines restricting the presence of lectins in food, but the FDA does provide recommended cooking practices prior to consuming legumes. Naturopathy may be safe but one should see the suitability, tolerability, palatability, digestibility etc. According to Lucretius "One man's food is another man's poison" food tolerable to one individual may be toxic to others. In fact, it is our individual genetic inheritances that determine how and to what degree lectins can affect us. Tolerance or intolerance to all kinds of foods is predetermined as per the genetic constitution starting from onset of life at womb of the mother. In view of the results observed on the edible food interactions with blood group antigens to be used for double blind placebo studies, we suggest the following measures/ recommendations should be considered before preferring the intake of raw juice of different plants and plant products/ parts (Table 1) for avoiding unwanted consequences with components present in the raw vegetables on the gut as well as health of an individual: (a) Ratio of different ingredients (i.e Water, salt/ sugar/ ice/spices powders etc) as per the recommendations of the nutritionists, (b) Moisture content in various fruits/ vegetables, (c) Homogeneousness of different states of mixture of plants/ plant parts, (d) Suitability to individual, (e) Quality/ Quantity/ impurities/ ripening status/ stability/ susceptibility to fungal spores/ Safety of the food, (f) Fiber/ mineral content, (g) Cultivation, serving process, colors and dyes, food adulterants, (h) Xenomic impurities, (i) Period of warm/ cooling treatment etc, (j) Diagnostic history on intolerance/ allergy status of foods to every individual . Our investigations will be useful for development of potential tools for specific drug targeting, Bio-adhesion applications, lectin blocking agents as drugs, Better food for good health and blood type diet.

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