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AYURVEDIC IMMUNOMODULATORY DRUGS SHOWING PHARMACOLOGICAL EFFECTS IN HEALTHCARE SYSTEM

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ABSTRACT

Ayurvedic system of medicine display a wealth of pharmacological properties. The ayurvedic system of medicine is one of the oldest systems of medicine and includes various ethno pharmacological activities such as immunostimulation, tonic, neurostimulation, anti-ageing, antibacterial, anti-viral, anti-rheumatic, anticancer, adapt genic, etc. The present review focuses on plant profile, pharmacological activities especially immunomodulation, uses (Traditional and medicinal), side effects and marketed products, And also the survey of all people who are aware, and what they consume for boosting immunity. The whole plant as well as plant parts such as the Fruit of piperlongum are used traditionally & is a flowering vine in the family Piperaceae. Asparagus racemosus is an important medicinal plant of tropical and subtropical India of family Liliaeceae. Liquorice is the most widely used herb from the ancient medical history of Ayurveda as a medicine as well as a flavoring herb with family leguminosae Guduchi is a well-known immune-modulator herb used in the correction of auto immunity of family Menispermaeceae. Turmeric is an Indian rhizomatous herbal plant (curcuma longa) of the ginger family zingiberaceae of well-known medical benefits. The sources of review paper were PubMed, research gate, Science Direct, kokate (BOOK). However Research has been done from ancient time and various research papers are published so awareness of these drugs and ayurvedic drugs should be done for betterment of health care system.

KEYWORDS: Piper Longum, Asparagus racemosus, Glycyrrhiza glabra, Tinospora Cardifolia, Curcumin, Ayurvedic Drugs, Plant profile, MOA, Immunomodulatory Effects, Pharmacological Effects.

INTRODUCTION

The Indian Ayurvedic system of medicine display a wealth of pharmacological properties. The Ayurvedic system of medicine is one of the oldest systems of medicine and includes various ethno pharmacological activities such as immune-stimulation, tonic, neuro-stimulation, anti-ageing, antibacterial, anti-viral, anti-rheumatic, anticancer, adapt genic, etc.

1. An entire section of the Material Medica of Ayurveda is devoted to "Rasayana", drugs reputed to enhance body resistance.
2. Listed as a class in the texts of traditional Indian Medicine literature, Rasayana consists of a number of plants reputed to promote physical and mental health, improve defense mechanisms of the body and enhance longevity.
3. A number of medicinal plants as Rasayanas have been claimed to possess immunomodulatory activity, e.g., Tinospora cordifolia, piper longum, asperegous racemous, glycyrrhizia glabra, Curcumin.
4. They can depress or potentiate the host's capacity to resist infection and tumors non-specifically, or react specifically to a foreign substance.

Immunomodulators act on the complex network of mechanisms of the immune system in a way not yet fully elucidated.[1]

Immune system is a complex system including cellular and molecular components which provide defense against infectious agents. The human body contains the organs of the immune system which protects against diseases. It plays a key role to maintain health and pathogenesis. It also protects the body from harmful substances, germs, and cell changes (neoplasm). The key player in the immune system is the white blood cells, which can travel throughout the body through the blood vessels.[2]

Immune system components

- Specific cells - lymphocytes, macrophages, etc., originate from precursor cells in the bone
- Marrow and patrol tissues by circulating in either the blood or lymphatics, migrating into connective tissue or collecting in immune organs.

- Lymphatic organs- thymus, spleen, tonsils, lymph nodes, Peyer's patches, Red Bone Marrow
- diffuse lymphatic tissue - gut-associated lymphatic tissue, mucosa-associated lymphatic tissue, skin-associated lymphatic tissue & collections of lymphocytes and other immune cells.[3]

Types of immunity

1. Innate Immunity or Natural or Non-specific Immunity.
2. Acquired Immunity or Adaptive Immunity.

1. Innate immunity or natural or Non-specific immunity:

Innate immunity represents the first line of defense to an intruding pathogen. It is an antigen-independent (nonspecific) defense mechanism that is used by the host immediately or within hours of encountering an antigen. The innate immune response has no immunologic memory and, therefore, it is unable to recognize or "memorize" the same pathogen should the body be exposed to it in the future. Innate immunity can be viewed as comprising four types of defensive barriers: anatomic (skin and mucous membrane), physiologic (temperature, low pH and chemical mediators), endocytic and phagocytic, and infammatory An important function of innate immunity is the rapid recruitment of immune cells to sites of infection and infammation through the production of cytokines and chemokines (small proteins involved in cell–cell communication and recruitment).[4]

2. Acquired immunity or adaptive immunity:

It is antigen-dependent and antigen-specific and, therefore, involves a lag time between exposure to the antigen and maximal response. The hallmark of adaptive immunity is the capacity for memory which enables the host to mount a more rapid and efficient immune response upon subsequent exposure to the antigen. The primary functions of the adaptive immune response are: the recognition of specifc "nonself" antigens, distinguishing them from "self" antigens; the generation of pathogen-specifc immunologic efector pathways that eliminate specifc pathogens or pathogen-infected cells; and the development of an immunologic memory that can quickly eliminate a specifc pathogen should subsequent infections occur.[4]

a) Acquired active immunity

1. It is the resistance developed by an individual as a result of an antigenic stimulus of invading Pathogens or vaccine. This immunity is acquired by activating immune system of the body and Results in production of antibodies.

It is of two types

I. Natural acquired active immunity:
II. Artificial acquired active immunity:

b) Acquired passive immunity: Passive immunity is acquired when ready-made antibodies are received by the body. Passive Immunity can be acquired either naturally or artificially.

I. Natural acquired passive immunity:
II. Artificial acquired passive immunity:

Immunity disorders – The Immune System can be under productive when it Fails to Recognize abnormal cells as cancerous cells or it can be over protective and cause other types of difficulties.

- **Allergies:** Hypersensitivity of the immune system to relatively harmless environmental Antigens – the immune system reacts to an outside substance that it normally would Ignore- allergy types (Food, dust, mould, seasonal), symptoms and signs (Skin rash, Itching, bumps, sneezing.
- **Autoimmune disorder:** A condition that occurs when the immune system mistakenly Attacks and destroys healthy body tissue- more than 80 different types – The immune System can't tell the difference between healthy body tissue and antigens. The result is an immune response that destroys normal body tissues. This response is a Hypersensitivity reaction similar to the response in allergic conditions Examples of Autoimmune (Or immune related) disorders include Addison's disease, Celiac disease –(Gluten-sensitive enteropathy), Graves' disease, Hashimoto's thyroiditis, Multiple Sclerosis, Pernicious anemia, Systemic lupus, Type I diabetes.

Immunodefficiency virus-For individuals with severe immunodeficiency, a successful bone marrow transplant is a standard life-saving treatment, using donor cells that do not harbour the dangerous mutation, or their own cells modified by genetic engineering to correct the defect.[5]

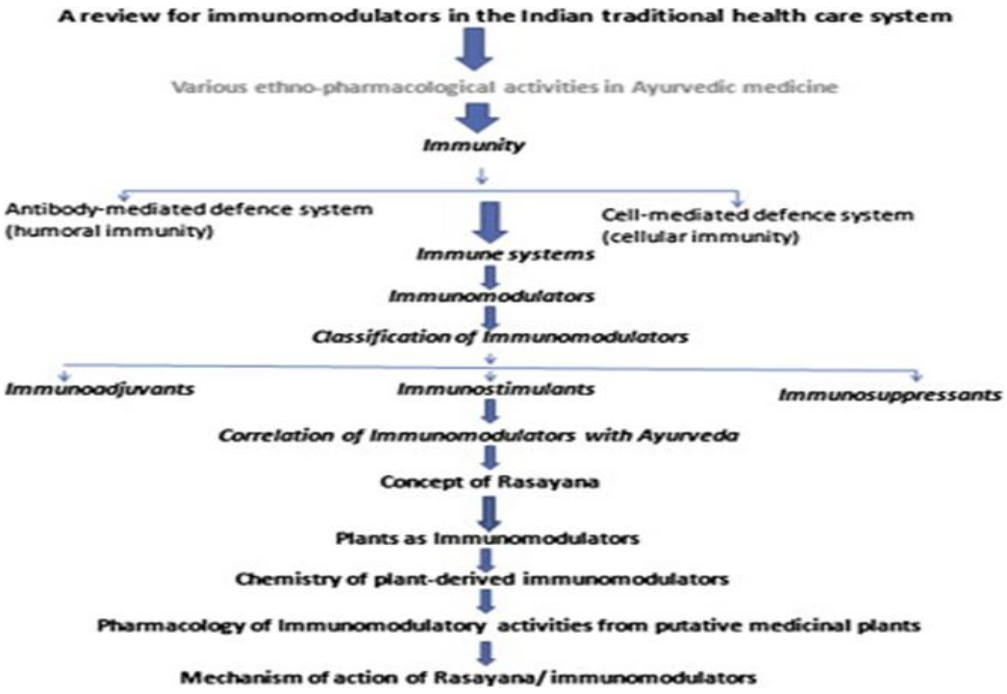
- (HIV) –HIV infection cripples the immune system, producing profoundly immune compromised individuals. Before the development of effective anti-retroviral therapy, HIV that reached the stage of AIDS was a death sentence.[5] It Infects Th cells and impairs other immune system responses indirectly.[4]
- AIDS – (acquired immune deficiency syndrome) is the final stage of HIV disease, Which causes severe damage to the immune system.

Side effects of immunomodulator drugs: There are various side effects are associated with the use of these drugs i.e. Pulmonary toxicity, Myelo suppression, Alopecia, Increased risk of infection, Hepatic fibrosis, Lymphoma (Epstein–Barr virus associated), Nephrotoxicity, neurotoxicity (tremor, headache, motor Disturbances and seizures), GI complaints, hypertension, hyperkalemia, hyperglycemia, and Diabetes, Renal dysfunction, tremor, hirsutism, hypertension, hyperlipidemia, gum hyperplasia, Hyperuricemia, hypercholesterolemia, nephrotoxicity, hypertension, diabetogenic, Elevated LDL cholesterol etc.

Mechanism of action of ayurvedic immunomodulator: Plants and minerals have been used since ancient times for the treatment of many ailments and diseases.[6] Ayurveda immunomodulators are the immunomodulators which stimulates or suppresses the components of immune system including both innate and adaptive immune responses.[1] Drugs are rich in flavonoids, vitamin C, or the carotenoids can enhance immune function. The flavonoid-rich herbs may also possess mild anti-inflammatory action. Their beneficial effect can be named as immunomodulatory as well as immune-stimulant action. It can promote the activity of lymphocytes, increase phagocytosis, and induce interferon production. For eg, Giloy is one of the most remarkable plants that can effect strongly on immune system. Primary targets of the Immunostimulant are T or B lymphocytes or the complement system, increase in phagocytosis by macrophages and granulocytes plays a central role in immunostimulation.

Macrophages activation is important for stimulating agents to remain in contact with the reactive cell. The second most important role is the stimulation of T lymphocytes, which can be achieved either directly or indirectly, via macrophages.[8] Immunostimulatory activity was achieved by proliferation of lymphocytes and macrophage activation assays. They are showing lymph proliferative and macrophage-activating properties reinforces the rationale of the use of natural drug preparations in several Ayurveda medicines for immunomodulation.

Mechanism of Action[1]



Example of ayurvedic immunomodulatory drugs enhancing immunity

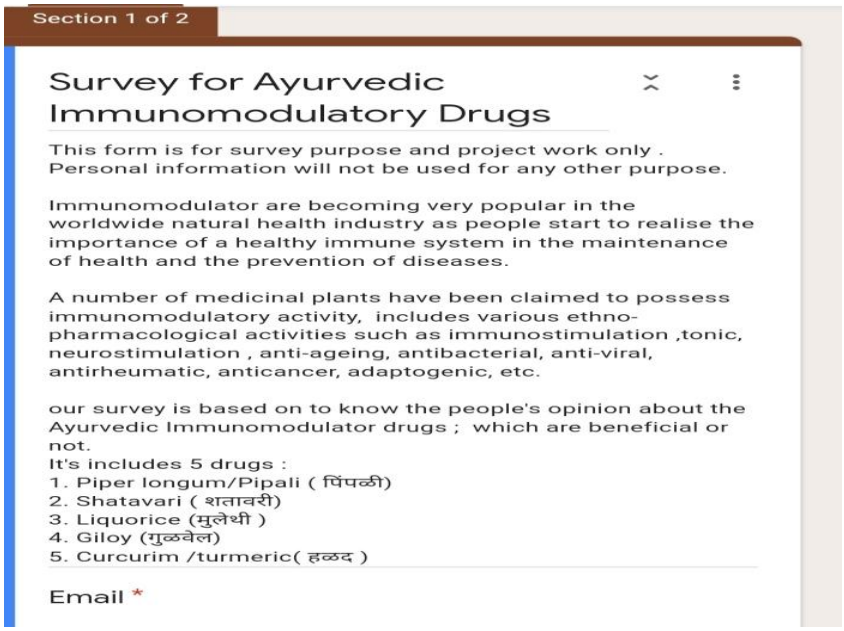
NO	Drugs	Biological Source	Family	Chemical Constituents	Uses
1	Piper longum	It obtained from flowering vine.	Piperaceae	Alkaloids & amides, Ligans, Esters, Volatile oils.	Immunomodulatory, Anti diabetics, Anti-cancer, Anti inflammatory.
2	Shatavari	The shatavari is derived from dried roots of asparagus racemosus wild.	Liliaceae	Alkaloids, Steroids, Flavonoids, Dihydrophenanthrene Derivatives	Anti-ulcer, Cure gastric problem, Anemic patient, Female reproductive health.
3	Liquorice	It is consist of dried, unpeeled roots and stolon part of Glycyrrhiza Glabra.	Leguminose	Triterpenoids saponin, Glucose, Sucrose, Asparagine, Flavonoids	Iron deficiency, Anti inflammatory, Anti-viral, Antibiotic, Anti diuretics
4	Guduchi	These are dried leaves and stem pieces of woody climber Tinospora	Menispermaceae	Alkaloids and glycosides, Sesquiterpenoids, Aliphatic compounds, Diterpenoids lactose	Anti diabetics, Anti-cancer, Dyspepsia ,vaginal and urethral discharges, Allergic rhinitis activity.

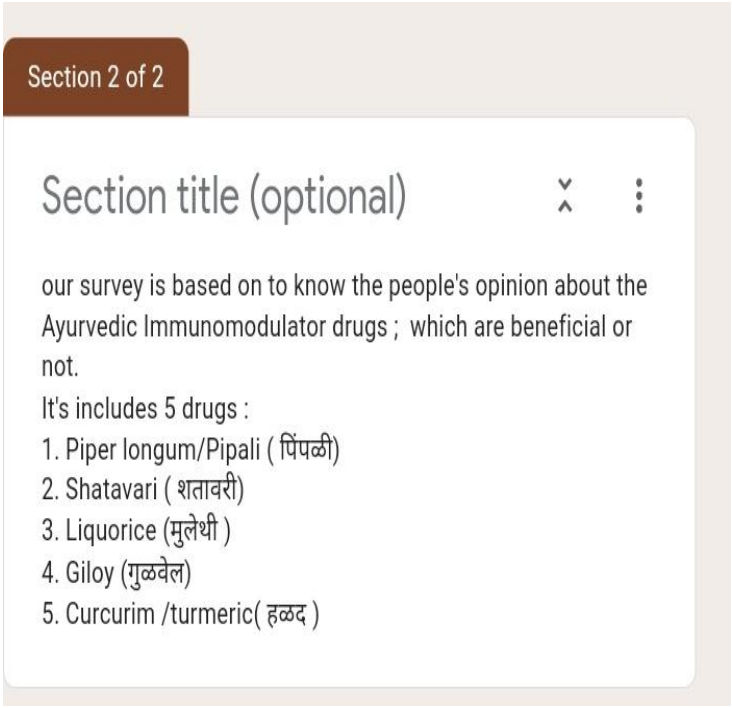
		cardifolia.			
5	Turmeric	It consist of curcuma Longa lin.	Zingiberaceae	Curcumin, Desmethaoxycurcumin, Ethanal Extract, Camphene, Resins and Ar turmerone	Osteoarthritis, Menstrual problem, Hay fever, Anti inflammatory, Bacterial infection/ wounds.

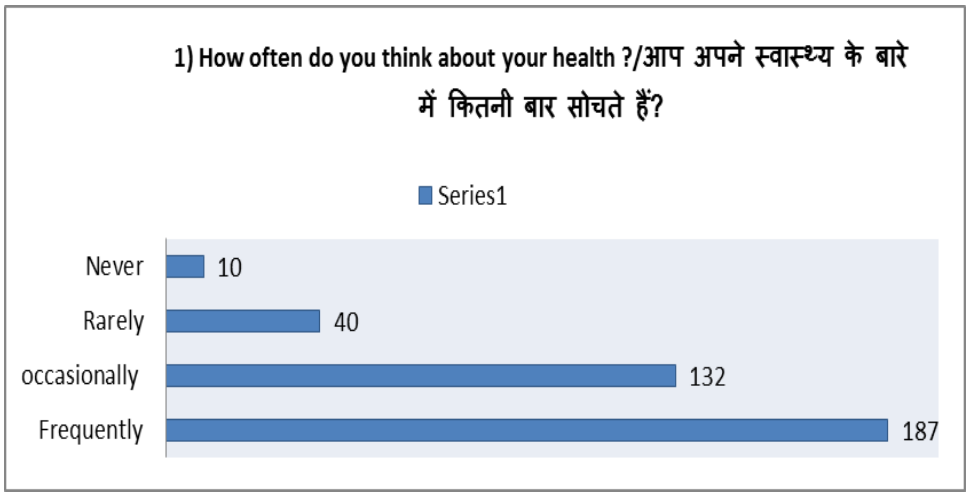
Survey

This form is for survey purpose and project work only. Personal information will not be used for any other purpose. For some questions we have given multiple marking options. our project is based on survey of Ayurvedic immunomodulatory drugs showing pharmacological effects in health care system and also of people who uses this types of drugs for their benefits and which drug they prefer more and more(for immunity & for any other purpose).In this project we have taken five drugs piper longum, shatavari, liquorice, giloy, curcumin and for each drug we mentioned plant profile, mechanism of action, pharmacological, immunomodulatory effects, side,effects, marketed products(Individually). The Survey indicates that the surveyed population is almost aware about Ayurvedic drugs which are used for enhancing immunity and their importance of acting on it. Based on the survey we found that curcumin is the most used drug and the most preferred drug by the population. According to the population curcumin showed antioxidant, antibacterial, anticoagulant antivenom and anti- inflammatory.

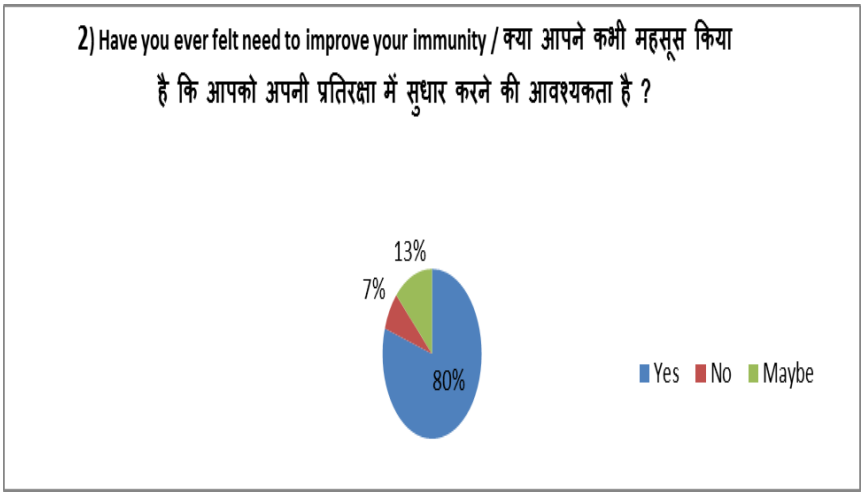
Survey-form



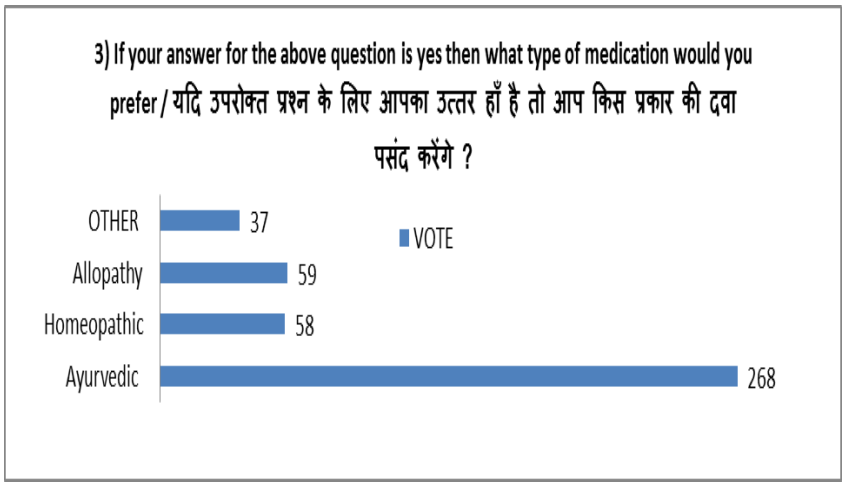




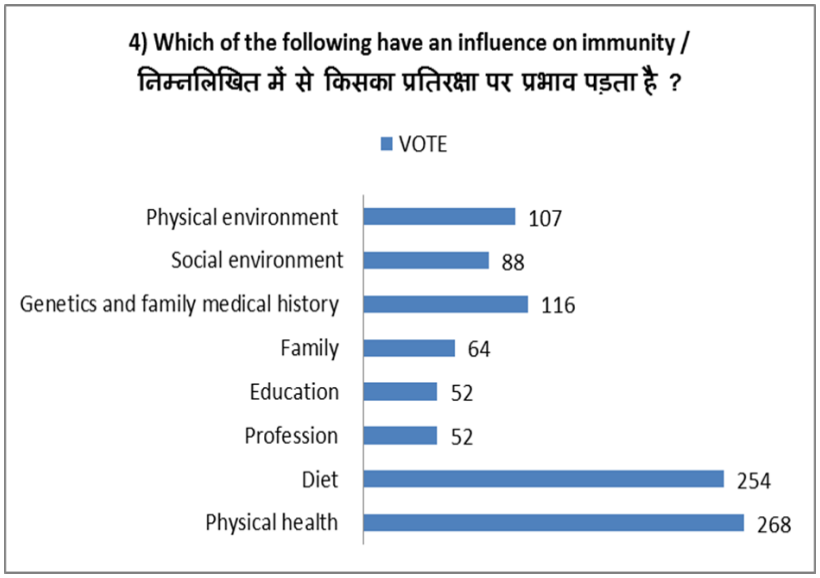
1. The above bar graph represents the number of a people who think about their health. Here the given options were frequently, occasionally rarely and never. from above given data we found that 187 people think frequently which is high, 132 people think occasionally, the number of people who think rarely is 40,and the minimum number of people who never think is 10.



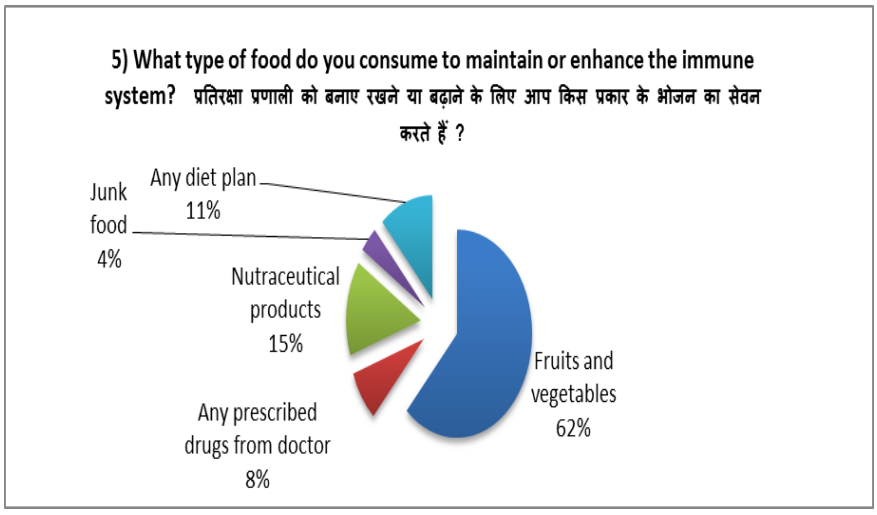
2. The above pie diagram represents the people who felt a need for improving their immunity and it is given in percentage form. The options which were given were yes, No and Maybe So, From above data we found that 80% of the people felt need of improving immunity while 7% people never felt any need and 13% people are confused whether they felt any need or not.



3. The third question is slightly related to the second question and The above bar graph represents to the people who felt need for improving immunity and what type of medication they prefer for boosting immunity. The options were Ayurvedic, Homeopathic Allopathy or any other medication. From above data we found that 268 people prefer Ayurvedic medication which is very high and 58 people prefer homeopathic medication while 59 people prefer Allopathy and number of people who prefer any other medication is 37 which is very low.

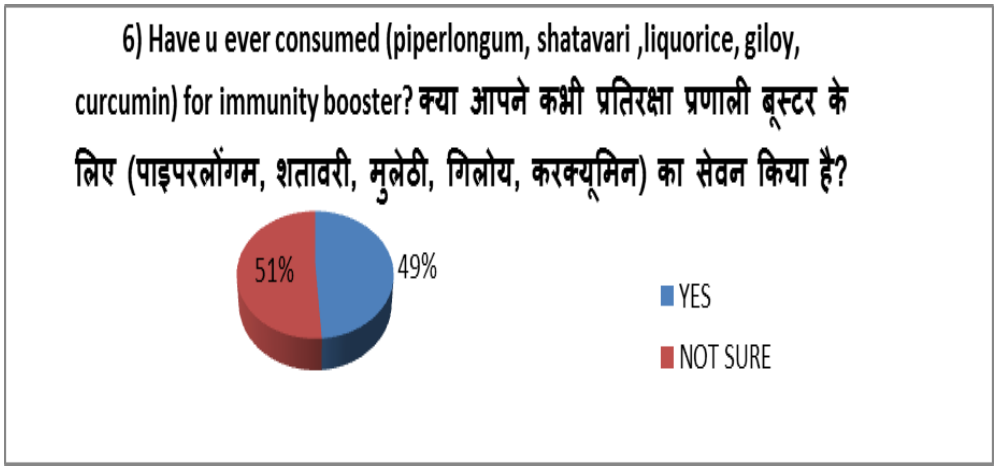


4. The above pie diagram represents the factors which have an influence on immunity and the options were Physical environment, social environment, Genetics and family medical history, Family, Education, Profession, Diet, Physical health. So let's start with the first factor that is physical health because 268 people think that physical health has influence an immunity, the next factor is Diet where 254 people think that it has an influence, 116 people the Genetics and medical history has an influence then 107 people think physical environment has an influence, 88 people think that social environment has an influence,64 people think family has an influence and last and we found equal number of people i.e 52 people think that education and profession has an influence on immunity.

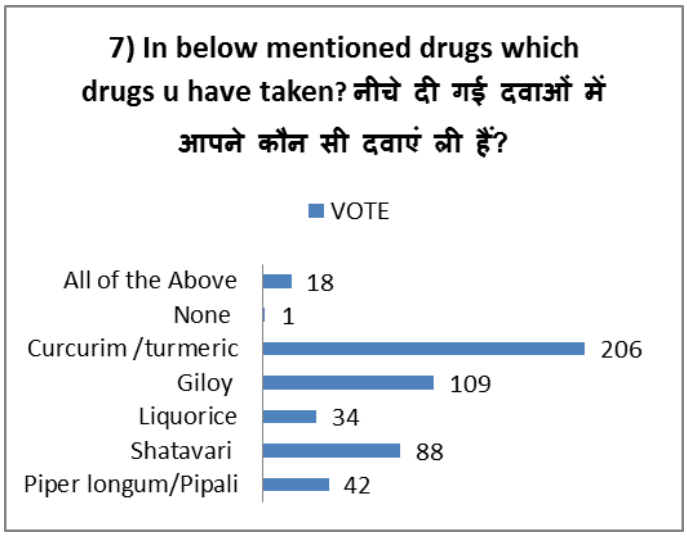


5. The above pie chart represents The type of food is consumed by the people for Maintaining & Enhancing the immune system. The options were Fruits and vegetables,

Any diet plan, Junk food, Neutraceutical Products, and any prescribed drugs from doctor. we found that 62% people people consume Fruits and vegetables, 15% people consume Neutraceutical Products,11% people prefer and consume Any Diet plan according to their convenient, 8% people consume Any other prescribed drugs from Doctor and 4% people consume junk food for immune system which is a reason to worry.

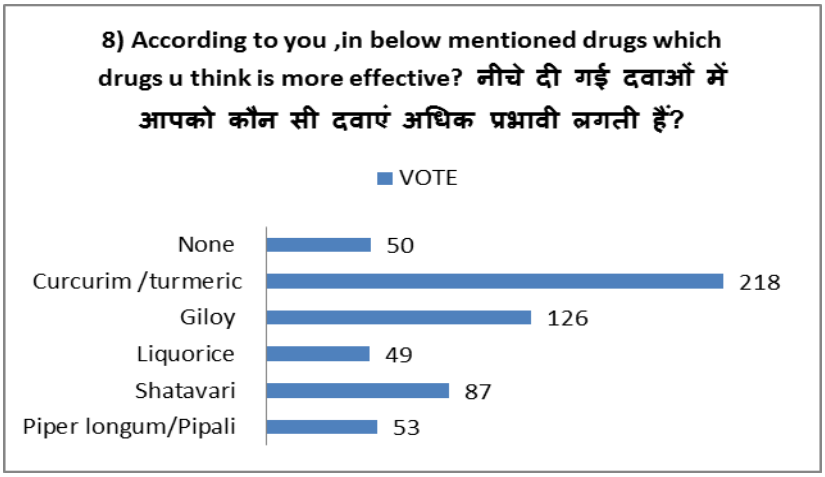


6. The above pie diegram represents the drugs like Piperlongum, Shatavari, liquorice, Giloy, Curcumin which have been consumed by people for immunity boosting & the options were Yes and Not Sure. We found that 49% people have consumed and 51% people are not sure whether they have consumed the above mentioned drugs.

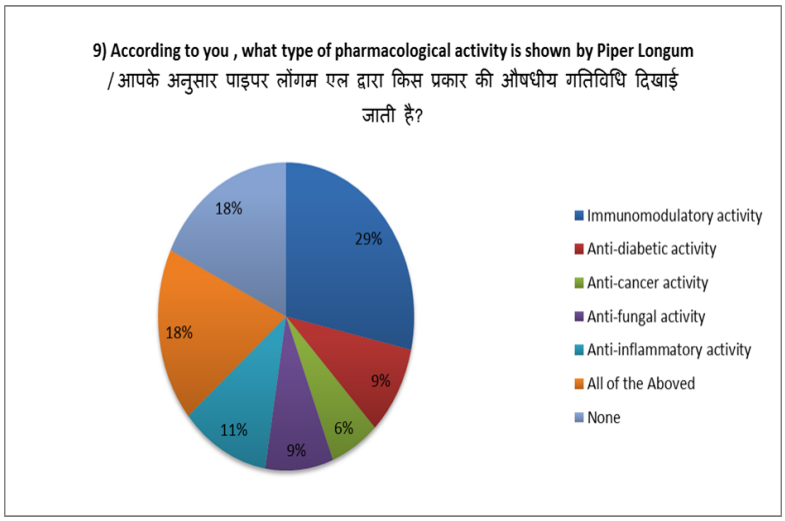


7. The above bar graph represents the people have taken drugs Piperlongum, Shatavari, liquorice, Giloy, Curcumin. We found that 206 people have consumed curcumin,109 people have consumed giloy, 88 people have consumed shatavari, 42 people have

consumed piperlongum, 34 people have taken liquorice,18 is the number of people who have consumed all the mention drugs, one is number of people who have no consumed any of the above mentioned drugs.

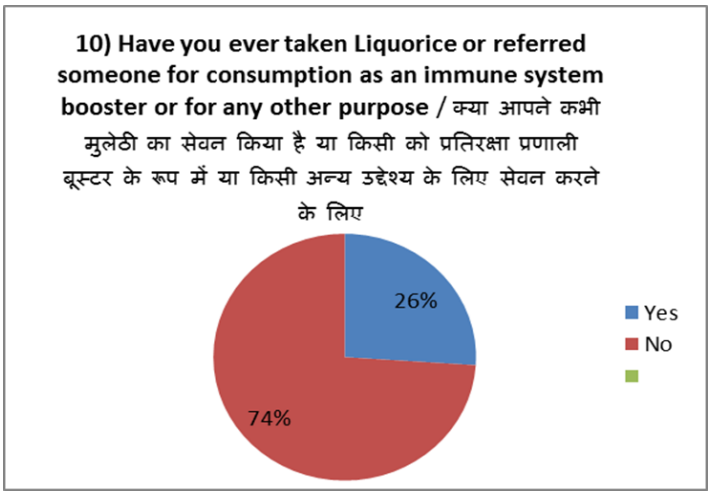


8. The above bar graph represents the mentioned drugs (Piperlongum, Shatavari, liquorice, Giloy, Curcumin) and which drug is more effective according to them. According to votes We came to know that 218 people think that curcumin is effective, 126 people think Giloy is effective, 87 people think Shatavari is effective, 53 people think piperlongum is effective and only 49 people think that liquorice is effective while 50 people are almost unaware and they don't think that above mentioned drugs are effective.

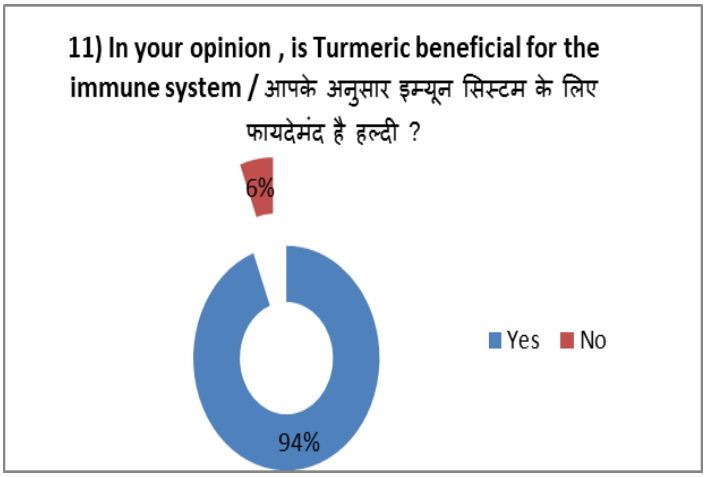


9. The above pie chart represents the type of pharmacological activities shown by piper longum, The options were Immunomodulatory activity, Anti-diabetic activity, Anti-cancer activity, Anti-fungal activity, Anti-inflammatory activity, All of the above &

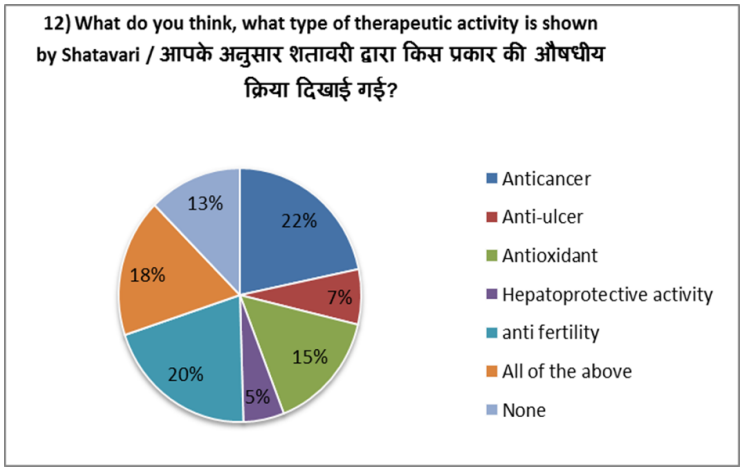
None. According to it, we found that 29% which is dark blue in colour represents the number of people who believe that it shows immunomodulatory activity, 9% which is red in colour represents the number of people who believe that it shows antidiabetic activity, 11% people which is moderate blue in colour represents the number of people who believe that it shows anti-inflammatory activity, 6% which is green in colour represents the number of people who believe that it shows anticancer activity and 9% which is purple in colour represents the number of people who believe that it shows antifungal activity, 18% which is orange in colour represents the number of people who believe that it shows all the above mentioned activities, 18% people believe that it shows no activity.



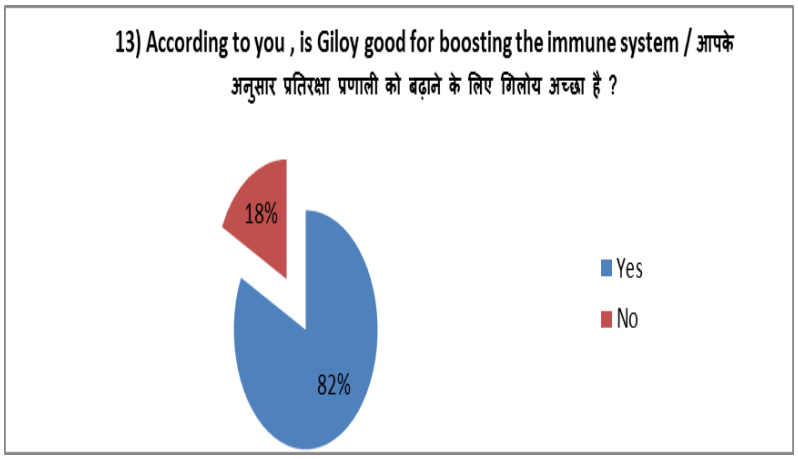
10. The above pie diagram represents the people who have reffered liquorice for consumption as immunity system booster or for any other purpose. we found that 26% people have reffered it an 74% people have not reffered it.



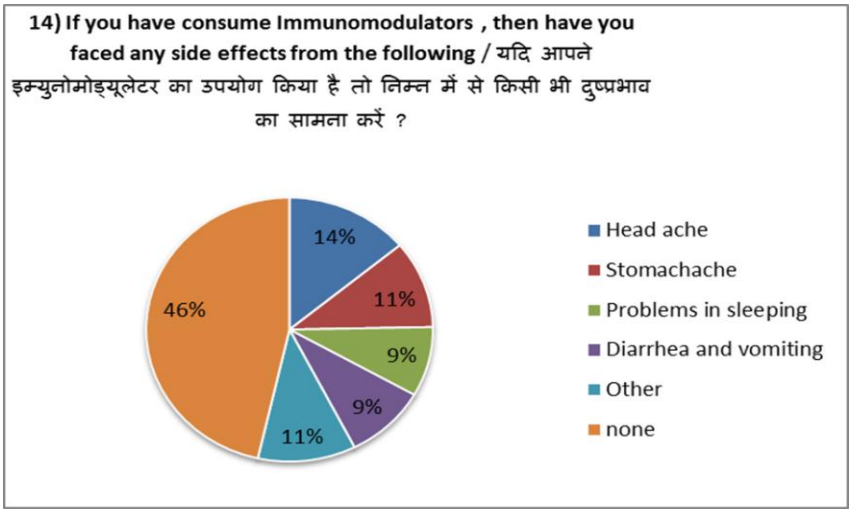
11. The above pie diagram is about turmeric, whether it is beneficial for immune system or not, so we found that 94% people have an opinion that it is beneficial and 6% people do not agree.



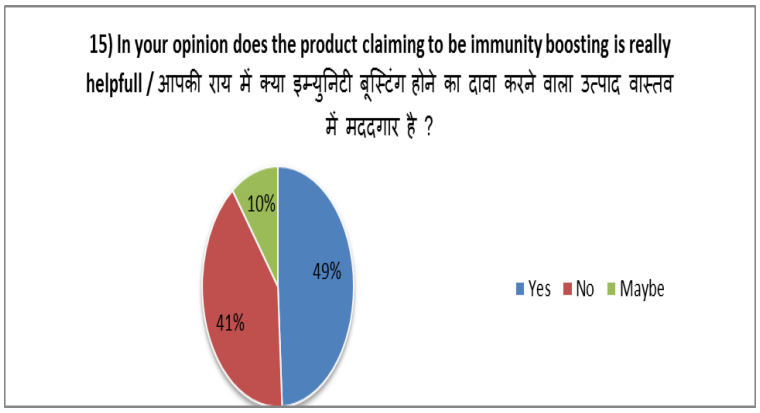
12. The above pie chart represents the type of therapeutic activities shown by shatavari, The options were Anti-Cancer, Anti- Ulcer, Antioxidant, Hepatoprotective, anti-fertility activity, All of the above & None. So from the given Information we found that 22% people thik its hows Anti-Cancer activity, 7% people think that it shows anti-ulcer activity, 15% people believe that it shows anti-oxidant activity, 5% people believe that it shows Hepatoprotective activity, 20% people think that it shows Anti-fertility activity, 18% people think it shows All of the above mentioned activity and 13% people think that no activity is shown.



13. The above pie diagram is about the people's opinion regarding giloy, and we found that 82% people think that it is good for boosting immune system while 18% didn't find it good as well as useful for boosting immune system.



14. The above pie chart represents the people who have consume immunomodulators and if yes then they what type of side effects they have faced from the options like Headache, stomach ache, problems in sleeping, diarrhoea and vomiting, others and none. 14% people have faced headache, 11% people have faced Stomach ache, 9% people faced sleeping problems, 9% people have faced Diarrhoea and vomiting problems, 11% people have faced any other issues, 46% people faced no issues after consumption.



15. The above pie chart represents the opinions given by the people of the product which is claiming to be immunity boosting is really helpful or not. The options were Yes, No, May be. We found that 49% people claim that it is useful, 41% people don't believe and 10% people are confused whether it is really helpfull or not.

16. **Do you have any doubt regarding herbal immunomodulators / क्या आपको हर्बल इम्युनोमोड्यूलेटर्स के बारे में कोई संदेह है ?**

ANS: Most of answers are NO.

CONCLUSION

Modern medical healthcare in developing countries such as India is still a far reaching goal due to economic constraints. Only a few plants have been screened for immunomodulatory activities. From the above review, it is evident that there are several medicinal plants and marine products which have immunomodulatory activity but inadequate evidence does not allow their uses in clinical practice. The Ayurvedic system of medicines not only provides that alternative, but also scores over the side effects and cost factor of allopathic medicine. Immunomodulator are becoming very popular in the worldwide natural health industry as people start to realize the importance of a healthy immune system in the maintenance of health and the prevention of diseases.

Although awareness/daily use of drug is high, only a minority i.e. 7.2% of population think that natural drugs cannot used for enhance immunity which is not enough. Improving one's knowledge, accessing correct information, and regularly using natural drugs for enhancing immunity are key factors of survey. Various secondary metabolites, such as alkaloids, glycosides, saponins, flavonoids, coumarins, and sterols, exhibit a wide range of immunomodulating activity. Therefore, immunomodulatory agents will gain more importance in the future research of herbal medicine due to their high efficacy, low cost, and low toxicity.

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