

IMPACT OF NUTRACEUTICALS ON GUT – BRAIN AXIS IN CHILDREN WITH AUTISM: FOCUS ON FISH LIVER OIL AND L-CARNOSINE

Dissertation Submitted to



The IIHMR University, Jaipur

for the partial fulfilment for the award of the degree of

Master of Business Administration (MBA)

in

Pharmaceutical Management

By

Tejas Sharadrao Kitey

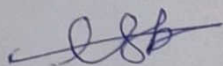
Under the Supervision and Guidance of

Dr. Ashok Peepliwal

2024

DECLARATION BY STUDENT

I hereby declare that this dissertation titled **“Impact of Nutraceuticals on Gut – Brain Axis in Children with Autism: Focus on Fish Liver Oil and l-Carnosine”** is the bonafide record of my original research work. I declare that it has not been submitted to any other university or institution for the award of any degree or diploma. Information derived from the published or unpublished work of others has been duly acknowledged in the text.

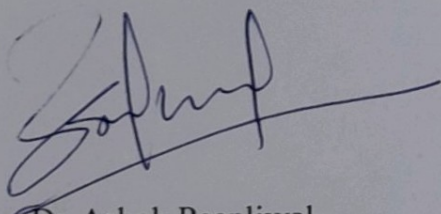


Tejas.S. Kitey

Date:05/07/2024

CERTIFICATE

This is to certify that dissertation titled “**Impact of Nutraceuticals on gut- Brain Axis in children with Autism: Focus on fish liver oil and L-carnosine**” Is a record of the research work undertaken by **Tejas S. Kitey** in partial fulfilment of the requirements for the award of the degree of MBA (Pharmaceutical Management) from the IIHMR University, Jaipur under my guidance and supervision and her approach to the research study has been sincere, scientific, and analytical.

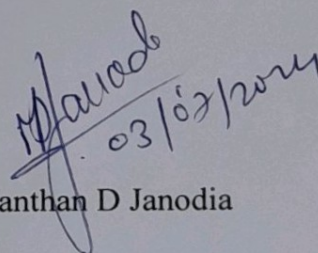


Dr. Ashok Peepliwal

Faculty Guide

IIHMR University, Jaipur

Date: 03/07/2024


03/07/2024

Dr. Manthan D Janodia

School Dean

IIHMR University, Jaipur

Date: 03/07/2024

ACKNOWLEDGEMENT

At the outset of my project report, I'd want to express my sincere gratitude to all the individuals who have assisted me with this project report. I would not have made any progress on the assignment without their strong leadership, participation, and consolation.

I am inexpressibly obliged to Mr. Saurabh Kumar, Associate Professor and Dean SPM, IIHMR University for his upright direction and support to finish this report. It is my radiant sentiment to place on record my best regards, and deepest sense of gratitude to Mr. Vinod Tejawani, Dean- Placements & Alumni Relations IIHMR University, and Dr. Ashok Peepiwal , Associate Professor, my Mentor at IIHMR University.

Finally, I'd like to express my gratitude to every companion who directly or indirectly assisted me in completing this assignment. Any omission from this brief affirmation does not imply a lack of gratitude.

Thank you,

Sincerely,

Tejas Sharadrao Kitey

Roll no. – 0458

TABLE OF CONTENT

Sr.No.	CONTENTS	Pg no.
1.	Abstract	VII
2.	Introduction	1-2
3.	Literature Review	3-17
4.	Method	18-20
5.	Suggestions and Recommendations	21-22
6.	Result	23-24
6.	Conclusion	25-26
7.	References	27-29

ABSTRACT

Objective:

Study the functioning of the nutraceuticals, vitamins, coenzymes, dietary changes, and phytochemicals in the management and treatment of ASD, which should have a dual effect: genetic changes, oxidative stress, and autoimmune response combined with the understanding of epigenetic processes relevant to such a neurodevelopmental disorder.

Methodology:

A systemic review on the existing literature and clinical studies, aimed at finding the answer to the efficacy of the various nutraceuticals approaches for the management of individuals with ASD, covered other fields: the roles of vitamins, coenzymes, and, to a lesser extent, dietary modifications, as well as possible phytochemicals, to lower oxidative stress and modulate immune and epigenetics responses. Data from this systematic review are presented using summarized data extractions from peer-reviewed articles, clinical trials, and meta-analyses to describe evidence for the current state of the literature.

Results:

The review concluded with the identification of some vitamins (B6, B12, and D), coenzymes (CoQ10), and dietary interventions (gluten-free and casein-free diets) that may have potential benefit for the management of ASD. Phytochemicals, curcumin, and resveratrol further show beneficial trends in reducing oxidative stress and inflammation, respectively. However, the results vary significantly between the studies and require stricter clinical trials with greater samples to draw firm conclusions.

Conclusion:

This makes nutraceuticals, such as vitamins, coenzymes, dietary modifications, and phytochemicals, a hopeful adjunct in managing ASD. Though confirmed in a few studies, greater exploration is needed to validate these benefits given their empirical nature and to work out standard regimes for treatment. Such a multidisciplinary approach, therefore, will carve a path for better overall benefit to people with ASD.

Key word:

Vitamins, coenzymes, dietary modification, and phytochemicals

Autism, Autistic disorder, oxidative stress, coenzymes, vitamins, nutraceuticals, dietary

CHAPTER 1

INTRODUCTION

What is Autism?

Autism, or autism spectrum disorder (ASD), is a complex neurodevelopmental condition that affects a person's ability to perceive and interact with others. It is characterized by difficulties in social interaction, communication, and repetitive behaviors. The precise causes of ASD remain unknown but are believed to result from a combination of genetic and environmental factors. Environmental influences during pregnancy or early childhood can also contribute.

Nutraceuticals are emerging as potential complementary therapies for autism, offering support by reducing inflammation and improving brain function, possibly due to omega-3 fatty acids in fish oil.

ASD typically manifests within the first three years of life, with a prevalence ratio of approximately 5 males to 1 female. Common comorbidities associated with ASD include gastrointestinal disorders, dysbiosis, autoimmune conditions, intellectual disabilities, and seizures.

Among the ASD spectrum, autism is a severe condition, characterized by significant impairments in social interaction and communication development, alongside highly restricted repetitive behaviors and specific profiles. About 85% of individuals with autism have idiopathic or primary autism, where the exact cause is unknown. Multifactorial and multifunctional causation of autism entails genetic factors, gastrointestinal issues, inflammation, reduced detoxification abilities, mitochondrial dysfunction, possible iatrogenic causes, including vaccinations and food additives.

Multiplex families, families that have more than one child with autism, are also a sibling of individual with autism. An increased risk of having autism is reflected with 20 to 30 times of the risk compared to occurrence in general population. Heritability is often very high up to 90%, and cases of autism have a strong genetic component. Environmental stressors during the perinatal period can contribute to the disorder in individuals with a specific genetic predisposition.

CHAPTER 2

LITERATURE REVIEW

The gut-brain axis is a relevant bidirectional interchange pathway connecting the gastrointestinal tract to the central nervous system in maintaining cognitive functions and mental well-being. This interaction takes place not only at a cellular level but also through biochemical interaction via neural, hormonal, and immunological pathways. The gut-brain axis is currently emerging as a crucial factor in the background of neurodevelopmental disorders, such as autism spectrum disorder, through recent findings. Nutraceuticals, derived from "food sources [and] providing health benefits," have now been cited in the medical literature as having a potential role as adjuvant therapies in ameliorating symptoms of autism, not only through mechanisms relating to gut and brain functions but also modulating the gut-brain axis. This review of existing literature was done to assemble available research on effects of nutraceuticals on the gut-brain axis in children with autism, focusing on fish liver oil and L-carnosine.

Fish liver oil is rich in omega-3 fatty acids, primarily eicosapentaenoic acid and docosahexaenoic acid. These omega-3 fatty acids are essential elements for the neuronal membrane; they have an anti-inflammatory effect useful in neurotransmission and have been observed, in meta-analysis, to favor hyperactivity, social skills, and repetitive behaviors in individuals with ASD. The anti-inflammatory use of omega-3 fatty acids is particularly pertinent in ASD, where neuroinflammation is

The higher dose of omega-3 fatty acids in some research studies may help decrease brain inflammation, especially because inflammation is one of the factors that can have such an effect on the brain. Dosages used in research studies vary but are typically between 1 and 3 grams daily. Fish oil is generally safe, and it should be purchased from a reputable company to avoid mercury and other impurities in the products. Research on optimal dosing and safety is required to determine long-term effects of fatty oil supplementation. It takes around three to four hours for omega-3 fatty acids from supplements to get into the bloodstream, although longer lasting effects may be obtained from the high quality ones. Other than these stuff, omega-3 fatty acids, DHA and EPA can also be naturally found in some good fatty cold water fish such as salmon, anchovies, and mackerel. Having these kinds of fish in one's diet once a week or at least 1-2 times a week will also aid in consuming an adequate intake of omega-3s. Another good source of omega-3 fatty acids can be found in some dietary sources such as flaxseeds, nuts, and chia seeds, which provide an alternative supply of the beneficial compound for the overall benefit of the body.

L-Carnosine is a dipeptide of β -alanine and histidine, well known for its antioxidant

effects, and found to be uniquely enriched in tissues of the brain and muscles. It buffers R-S and involves in modulating various neurotransmitters, playing a critical role in neuronal

Show More However, some researches determine the effect of L-carnosine in children, which shows an impressive result with impairment in language ability, social behavior, and function after supplementation. Of most interest in ASD is the antioxidative potential of L- carnosine, entailing oxidative damage by lessening it, L-carnosine protects neuronal cells and enhances the functions of neurotransmitters. More so, L-carnosine

Modulates GABAergic and glutamatergic neurotransmission, important for maintaining the balance between excitatory and inhibitory signaling in the brain (Karakas et al., 2013). Common dosages used in research fall within the 400–800 mg per day range. Such dosages have to be used judiciously, especially for the long term, and only with the consultation of health care providers.

Integrating Nutraceuticals into Autism Management

Thus, the use of the nutraceuticals on the lines of fish liver oil and L-carnosine in the management of autism features would call for an individualized approach, recognizing the variability of ASD. Exactly how a person responds to these nutraceutical interventions most likely depends upon genetic, environmental, and lifestyle factors. For this reason, biomarker-guided strategies to assess inflammation, oxidative stress, and nutritional deficiencies can provide further customization to effectively address the individual needs. Nutraceuticals might probably be another supportive management strategy that could partially complement other therapeutic modalities of autism spectrum disorder, including behavioral therapies, pharmacological treatments, and dietary adjustments. The combined action of multimodal approaches may be additive or even synergistic, thereby enhancing general therapeutic outcomes

Comorbidities in Autism Spectrum Disorder: -

Gastrointestinal (GI) symptoms are frequently reported among children with autism spectrum disorder (ASD). Studies have consistently shown that autistic individuals often experience more severe and numerous GI issues compared to their non-autistic children and healthy ones. For instance, in a small study involving the total number of autistic children, non-autistic siblings. A preschooler similarly found that ASD patients suffered from GI problems more frequently than their healthy peers. Additionally, ASD patients with GI symptoms exhibited more anxiety, other somatic complaints, and reduced social interaction compared to those without GI issues.

Constipation is the common GI symptom observed in autistic children, with a noted connection in rigid-compulsive behavior and constipation. GI symptoms in autistic children have been linked to increased tantrums, aggressive behavior, and sleep disturbances, exacerbating behavioral having no symptom of GI disease. One review suggested that sleeping disorder may to abdominal functionality.

Autistic children exhibit differed metabolism and assimilation of disaccharides in their gut linings. Lower mRNA levels of disaccharidases in the brush border of the ileum, such as lactase, maltase glucoamylase, and sucrose isomaltase, result in decreased gene expression. Additionally, the sodium-dependent glucose cotransporter (SGLT1) and the glucose transporter 2 (GLUT2), responsible for transporting glucose, galactose, and fructose across the enterocyte membranes, have significantly decreased mRNA levels in autistic children. This impaired absorption in the small intestine causes an increased amount of mono- and disaccharides to reach the large intestine, where they are fermented by bacteria.

Consequently, this leads to a changed microbial composition in the gastrointestinal tract., with bacteria fermenting low-molecular sugars outcompeting those that degrade polysaccharides.

Increased Gut Permeability:

Elevated intestinal permeability has been noted in individuals with autism spectrum disorder(ASD), as indicated by higher blood lactulose levels following oral intake. Both types of conditions of siblings demonstrate increased gut permeation compared to others. The increased permeability is probably because barrier-forming proteins are less effective, and there is a higher expression of pore-forming proteins in the tight junctions of the lining.

These alterations were identified by analyzing mucosal samples from the small intestines ofautistic children compared to non-autistic children.

The changed gut permeability in autistic individuals might also be associated with a decreased presence of Lactobacillus strains, which are crucial for maintaining the integrity of tight junctions in the intestinal barrier. The metabolites of bacteria, for instance, LPS, are likely to diffuse through the flimsy barrier more easily, hence leading to an induction of inflammation impacting on the brain by modifying cytokine levels.

Moreover, this increased intestinal permeability has been replicated in some non-autistic family members of autistic individuals, which rules out the notion that this condition may well be unique only as a consequence of ASD. Rather, heightened gut permeability must be considered a predisposing factor which, in concert with additional environmental factors, may contribute to the pathogenesis of the disorder.

FACTORS INFLUENCING THE GUT BRAIN AXIS

It is a complex and bidirectional communication system that comprises the central nervous system and the gastrointestinal tract. It is composed of neural, hormonal, and immunological signaling pathways. Up to now, the GBA has been regarded as playing a role in the disease quite neurologically unique—that is, autism spectrum disorder, a neurodevelopment disorder characterized by impairments in social communication and repetitive behaviors. Emerging information from this regard emphasizes that gut microbiota and gut health might affect brain function and behavior. It considers specific factors that appear to exert influence on GBA in the autistic population, for example, genetic, environmental, immunological, microbial, and nutritional factors.

Genetic Factors

Genetic predisposition plays a huge role in the development of ASD. Many genes identified in association with ASD have been found to be implicated in synaptic roles, neural development, and regulation linked to the immune system. Gene mutation and variation can influence gut microbiota composition, gut health, and vice versa, affecting the GBA.

1. Neuroligin and Neurexin Genes

Neuroligin and neurexin genes are key factors in the formation and maintenance of synapses. The mutations in these genes have been detected in ASD and could thus perturb synaptic signaling. Such disruptions might disturb their coordination, which would have an effect on general GBA functioning.

2. SHANK3 Gene

A second example is the SHANK3 gene, encoding a protein central to synaptic signaling: mutations in SHANK3 can cause affective gastrointestinal problems and changes in gut microbiota, which can, in turn, influence brain functioning and behavior through the GBA.

Environmental Factors

Hormonal and environmental factors may impact GBA, therefore contributing to ASD, especially during the prenatal and early postnatal phases of development.

1. Maternal stress and infections

Maternal stress and infections during pregnancy are associated with increased risks for ASD in offspring. These stressors may induce immune activation and inflammation, which affect foetal brain development and gut microbiota establishment.

2. Antibiotic Exposure

Early-life exposure to antibiotics seriously interferes with natural gut microbiota development and causes long-lasting alterations within the GBA that evidently affect brain and behavioral development and, subsequently, the development of ASD.

Immunological Factors

The immune system is involved in gut health and the regulation of the GBA, and immune dysregulation and inflammation are common in ASD.

1. Gut-Associated Lymphoid Tissue (GALT)

GALT is the most primordial part of defense mechanism in the gut, acting to control immune conditions toward gut microbiota and pathogens. Its disturbance can promote autoimmune inflammation and immune activation and hit GBA functions, eventually leading to ASD.

2. Interferons, Cytokines, and Inflammation

People with ASD have higher levels of pro-inflammatory cytokines. Such cytokines change the diffusible of the BBB and the walls of the intestines, hence changing the gut-brain communication and may contribute to ASD symptoms.

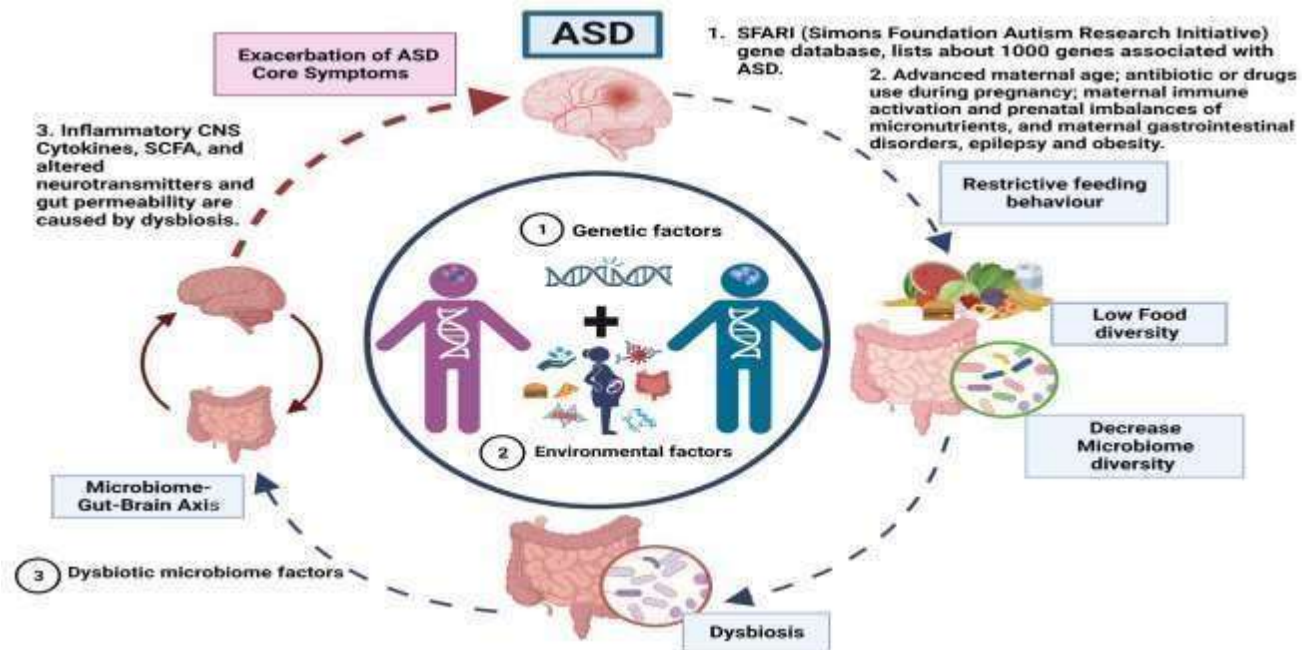


Fig: Process of Autism Spectrum Disorder

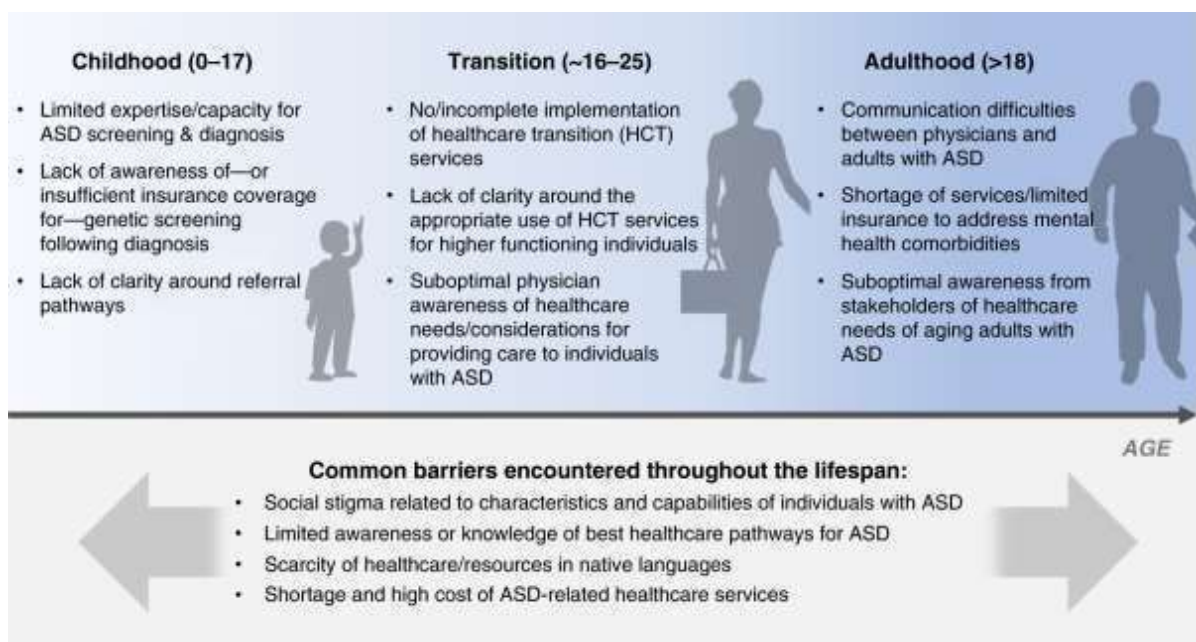


Fig : Complexities in Social Interactions in Various Stages of Ages.

OTHER ETIOLOGY OF GUT BRAIN IN TERM OF ASD

Autism spectrum disorder (ASD) is a neurodevelopmental disorder in social communication and behavioral alterations in approximately 1 in 54 children in the US. Up to now, emerging studies suggest a critical role of the gut-brain axis in ASD. The GBA is claimed to involve neural, hormonal, and immunological pathways, where the gut microbiota and the state of the gut could potentially influence brain function and behavior. Genetic factors are important in the development of ASD, with genes such as neuroligin, neurexin, SHANK3, and CNTNAP2 playing key roles in synaptic signaling and neural development, which may consequently alter the gut microbiota and GBA function. Prenatal and early postnatal environmental factors, which include maternal stress, infections, antibiotic exposure, and environmental toxins, also shape the GBA and might contribute to ASD pathogenesis.

The GALT dysregulation, including overall enhanced pro-inflammatory cytokines and autoimmune conditions, is an immunologic factor that is important for gut health and immune GBA regulation but is broadly represented in ASD with immune dysregulation and inflammation. The gut microbiota is a vast and very diverse community of trillions of microorganisms that regulate the GBA. Dysbiosis, including aberrations within specific bacterial groups such as Bacteroides and Clostridia, is common in cases of ASD and can impact the gut barrier integrity, immune function, and production of neuroactive compounds. Major dietary factors shaping the components of the gut microbiota and influencing the GBA include sensitivities to gluten and casein and the use of lactases.

The gut microbiota produces a number of neurotransmitters including serotonin, GABA, and dopamine, which are involved in gut-brain communication. In ASD this would change both in the production and function of these neurotransmitters. Integrity of BBB and gut permeability, which is also termed "leaky gut," are such critical mechanisms for control of GBA. Dietary interventions have been found to help in the facilitation improvement of gut health and rescue the symptoms of ASD. Interest-focused dietary interventions aside, some aspects that are valued in the study include probiotics, prebiotics, and, more recently, FMT. Still, there is a need, therefore, for their effectiveness and safety in this regard to be noted.

NUTRACEUTICAL AND AUTISM

"Food has moved beyond its traditional role to further becoming a potent determinant of health and wellness. This revolutionary change toward food as medicine has given birth to the concept of 'nutraceutical,' word first coined in 1989 by Victor. Nutraceuticals are foods, or food components like dietary supplements, that provide health benefits maintaining and promoting health and preventing and treating disease". Nutraceuticals are defined as substances that are part of food and provide medical or health benefits, including disease prevention and treatment. These encompass dietary supplements such as vitamins, minerals, and many more. Unlike typical dietary supplements taken in doses, nutraceuticals can modify conventional foods to achieve therapeutic outcomes, integrating seamlessly with traditional treatments to enhance health results. Their benefits include promoting gut health, reducing bodily toxin burdens, decreasing excitotoxicity, improving antioxidant stress, bolstering immune responses, and mitigating stress and environmental changes. These benefits are particularly significant in the context of autism management, where they can complement existing treatments to address the disorder's etiological complexity and overcome limitations of early interventions. The concept gained momentum in 1995 with the Defeat Autism Now (DAN) initiative, which united scientists, physicians, and parents in a campaign to improve autism treatment through research and practical interventions.

Nutraceuticals have shown promise in this area as well, and of different compositions being already marketed and some being even on record with anecdotal evidence of success in autism and similar neurological conditions. According to Transparency Market Research, the global market for nutraceuticals, valued at \$165.62 billion in 2014, is projected to grow at a compounded annual growth rate (CAGR) of 7.3%, approximately \$280 billion by 2021. This is primarily due to lifestyle changes and the high cost of traditional healthcare. Nutraceuticals are subject to varying regulatory standards in different countries, in the United States, for example, the barriers by government regulations are not so stringent as those followed for pharmaceuticals. Nutraceutical manufacturers have to comply with FDA good manufacturing practice regulations as an assurance of safety of their product, but they do not need to register their products and obtain FDA approval before marketing it in the market. This has created a political regulation space. Generally, including nutraceuticals in health strategies show brighter potential for disease prevention and health promotion with a scope that goes farther than supplying basic nutrition towards offering significant therapeutic benefits.

Gut Brain Axis And Role Of Nutraceuticals In Influencing The Mental Health Of Children's

Many think of the gut-brain relationship as one of the most fascinating and relevant connections that takes place in the human body, linking the central nervous system with the gastrointestinal tract. It represents a bidirectional communication system through neural, hormonal, and immunological pathways that interact to maintain homeostasis and govern a number of physiological functions. At the centre of this axis lies the gut microbiota, with trillions of organisms that live inside the GI tract—so important in health and disease. Major actors in the neural control of the gut-vascular mind axis, the vagus nerve—especially the longest cranial nerves—conduct these signals between the gut and the mind. These signals control functions such as digestion, mood, and immune responses. On mental well-being, as well as the gut health, a recent study highlights intrinsic effectiveness through assessment showing that produced metabolites, e.g., short-chain fatty acids, are anti-inflammatory.

properties with potential to affect brain function. Dysbiosis, an unhealthy balance of Intestinal microbiota dysbiosis has been associated with a number of mental states, some of them even beginning to take shape in childhood: anxiety, depression, and autistic spectrum disorders.

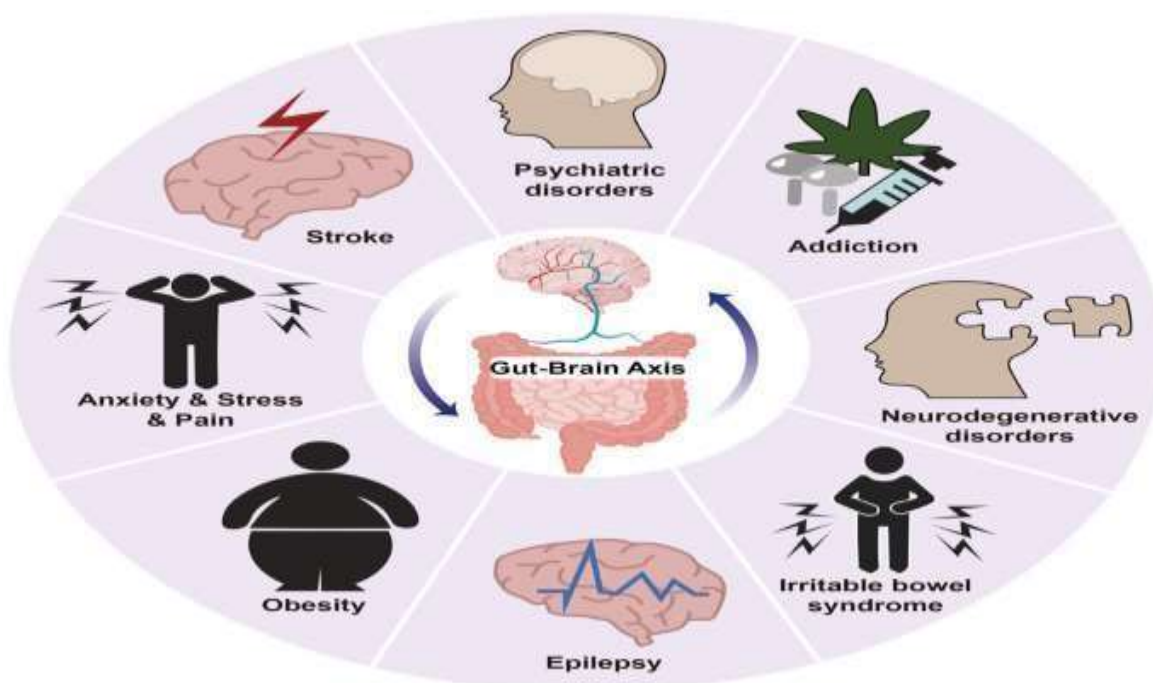


Fig:- Types of Diseases Caused Due to Abnormality in Gut Brain Axis.

For example, the gut-to-brain axis is much more crucial for a child than it is for an adult because of the on-going development and change that characterizes the brain. The results are long term effects on mental health and cognitive function; an example includes a relation between gut health and autism symptoms.

Several studies have shown that gut microbiota profiles in autistic children differ from neuro-typical children.

Two key constituents often referred to are the following: Omega-3 fatty acids and L-carnosine:

OMEGA 3 FATTY ACID

These are the most important EPA and DHA, oily essential fats found in fish oils. They are very important for the growth of the brain and its proper functioning, especially since they act as anti-inflammatory properties and have an effect on mental health. It is the cod fish liver oil that contains lots of omega-3 fatty acids and vitamins A and D. L-carnosine is the dipeptide formed by the combination of beta-alanine with the peptide histidine, which is widely recognized for its antioxidant potential, as well as the fact that potential therapeutic properties. With such great potential health benefits evidenced, fish-liver oil and L-carnosine have evoked immense interest in the area of brain-health, cardiovascular function, and anti-aging properties. This essay lays in detail to the composition of fatty acids in the fish liver oil and the properties and benefits of L-carnosine.

Fatty Acid in Fish Liver Oil

Fish liver oil is found to be high in the omega-3 fatty acid, which is attained with vital importance to numerous functions of the body. Basically, this consists of eicosapentaenoic acid and docosahexaenoic acid, which find paramount use within a number of functionality relating to the regulation of inflammation, cardiovascular health, and neural development.

1. Eicosapentaenoic Acid (EPA)

It is the long chain polyunsaturated fatty acid noted to possess 20 carbons with the five double bond compounds mainly alkenes (20:5, n-3). It is mainly used for its anti-inflammatory benefits and for the heart.

Anti-Inflammatory: EPA aids in the synthesis of cytokines and oxy radicals that are usually inflammatory eicosanoids. It consists of arachidonic acid (AA) that helps in reducing active production.

Antihypertensive properties: EPA reduces serum triglycerides, causes a drop in blood pressure, and improves endothelial function, the overall effects of which lower the risk of atherosclerosis and other cardiovascular diseases.

1. Docosahexaenoic Acid (DHA)

DHA is an omega-3 fatty acid having 22 carbon atoms and six double bonds; more precisely, it has 22:6, n-3. It is a major structurally important part for various parts of the brain, retina, and other cell membranes.

Brain Functionality: DHA is typically utilized for neurohealth, and cognitive functionality. It contributes to synaptical flexibility, hence aiding in the development of neurons.

Optic Function: DHA is a critical component of the retina, helped for visual acuity, and health of the eye.

Effect in anti-hyperlipidemia: it helps to reduce LDL and support heart health.

The constituent of Fish Liver Oil Vitamins A and D

It provides a source of vitamins A and D that is generally physiologically utilized.

Vitamin A: Helps in vision, immune function, cellular functionality; in fact, it shares a general composition in retinal.

Vitamin D: assists in homeostasis, absorption of calcium and phosphorus in the gut linings.

L-CARNOSINE

L-Carnosine is another dipeptidic compound that has reducing properties and functionality in children with autism. It will help in oxidative stress and neurotransmitter functionality in autism conditions. L-carnosine will improve communication skills, social well-being, and reduce hypersensitivity. Dosage 400 to 800 mg daily

1. Reducing Properties

It has antioxidant that helps cells from oxidizing properties forming the free radical. Protection against for the antioxidative properties - L-carnosine scavenges free radicals, reduces lipid peroxidation, and protects DNA damage from oxidizing.

Cellular longevity: through the mitigation of oxidative stress, L-carnosine contributes to cellular longevity and overall health.

2. Neurological Benefits

Support for brain health and cognitive function. L-carnosine uses multiple mechanisms, as illustrated in relevant studies.

Neuroprotection: Protects neurons from oxidative stress, excitotoxicity, and apoptosis

Cognitive improvement: a few studies have shown a neuroprotective action of L-carnosine against cognitive decay, but it's not clear yet and suggested a possible ameliorating in cognitive failure, especially for memory and learning, in conditions of oxidative stress and aging.

Future Research Directions

Further research efforts should be dedicated to coherent, large-scale, and randomized control studies to establish the real picture of the impact of nutraceuticals on the gut-brain axis in children with ASD. These studies should systematically examine optimal dosages, long-term safety profiles, and possible interactions with concurrent treatments. This might provide insight about mechanistic knowledge related to how such nutraceuticals are impacting neurodevelopment and behavior. Further research in these areas will pave the way for nutraceuticals that might be used to benefit those who have ASD.

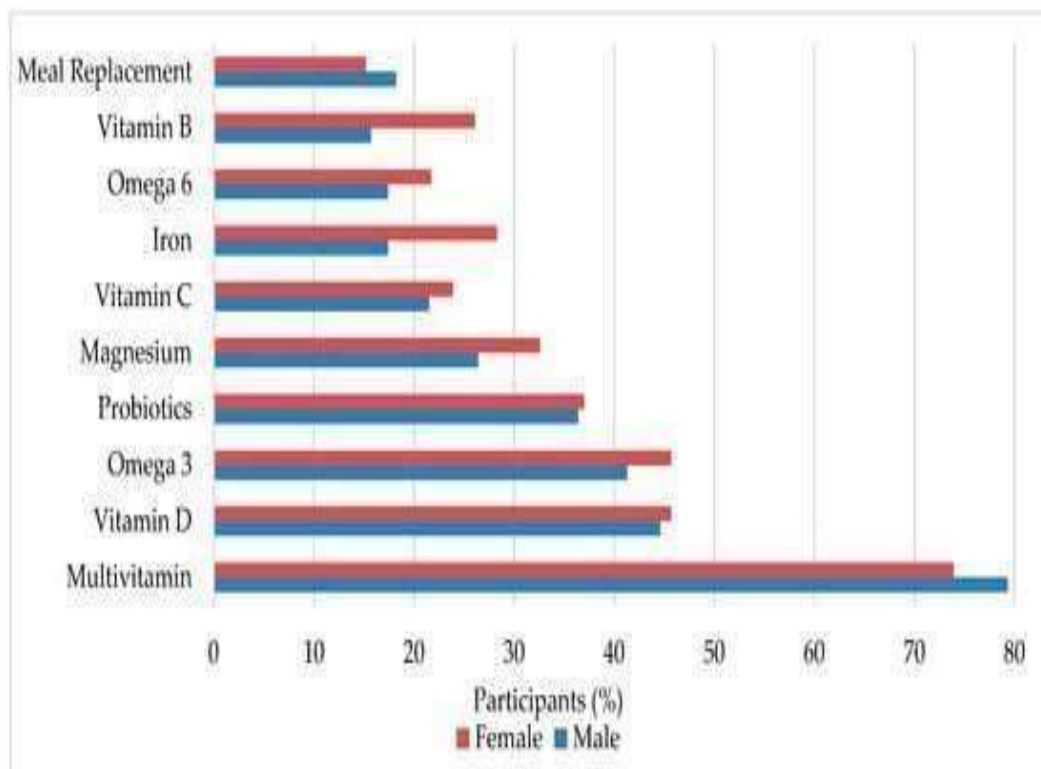


Fig : Intake of Components of Nutraceuticals in Male and Female.

CHAPTER 3

METHODOLOGY

In the academic discourse, phenomena are usually substantiated with reference to research works, case studies, and a variety of other scholarly works. These referents form the bases of credibility because they lodge empirical evidences and theoretical frameworks that anchor the polemical discussions and analyses in the realm of academic fields. Research papers, in essence, play an important role by bringing forth systematic investigations and findings based on methodical inquiry. They both give detailed accounts of procedures used, data collected, and conclusions arrived at and therefore contribute in depth to the body of knowledge in the respective fields.

Another major form of references is through case studies, which means in-depth examination of specific examples or situations. They offer context-specific reflective insight into the going-on of the real-world events, thus further assisting portray the ideal concepts practically. Case studies provide reflection of complicated and fine elements that broad theoretical debates may find difficult to grasp. Diachronic explications of such cases normally bring out the key factors, outcomes, and their implications for the knowledge thus enriched.

'References' on the second column of this table are the general category, which includes not only research papers and case studies but also textbooks, authoritative books, archival materials, and primary sources, each of which plays a different function in academic argumentation. Textbooks are a synthesis of basic knowledge and of classic theories and can perfectly provide complete and extensive general summaries of a certain field or subjects, which is suitable for the purposes of education. Authoritative books provide a good deal of insights into certain special aspects and their interpretations that are often done by authorities or scholars in that particular subfield.

Archival materials and primary sources are first-hand accounts and original data critical in historical research and empirical studies.

Together, these references provide the foundation of a strong academic investigation and discussion. They allow for a critical analysis of concepts, theories, and the results of measurements, and thus they support critical thinking and enlightened discussion in scholarly circles. By using different sources, credibility is built for the claims and knowledge is advanced in a cumulative manner. The plurality of this approach ensures scholarly conversations have reason and enrich in multiple perspectives. In this way, references do not apply merely to the sources of information; rather, they serve as the catalysts for intellectual exploration and discovery in the journey toward excellence in academia.

COMPETITOR BRANDS

In the Indian market, many brands are selling accessories containing L-Carnosine, Omega-3 fatty acids, thereby successfully capturing the needs of the consumers for health supplements to provide cognitive, cardiovascular, and other health benefits. These ingredients gained popularity for purported benefit in the realms of cell health, brain activity, and cardiovascular upkeep. Knowing the competitive landscape of these brands helps one take an informed choice based on the composition of the product and its quality. The nutraceutical market would undergo a huge surge and penetration on the basis of growing awareness of health, increased healthcare costs, and aging population. The modern-day consumer is proactive about health and looks for preventive care to stay well and manage chronic conditions. This gradual shift in consumer behavior creates demand for functional foods, dietary supplements, and fortified beverages.

This makes nutraceutical products safer and more targeted due to ongoing research and technological advancements. Market penetration, along with the growing trend of personalized nutrition, is pushed by regulatory support. Digitalization and e-commerce strategies will help the companies reach a wider customer base, thereby enabling access and convenience which are easier for the target customer. On this account, the changes in health needs and demands of the global diversity indicate that the nutraceutical market is going to fast expand.

List of Competitive Brands in India:

1. Amway Nutrilite
2. Himalaya Wellness
3. HealthKart
4. GNC India
5. INLIFE Healthcare
6. Abbott Nutrition (Ensure)
7. Healthvit
8. Zenith Nutrition
9. Herbalife Nutrition
10. Nature's Bounty

SUGGESTIONS AND RECOMMENDATIONS

Despite the encouraging findings, nutraceuticals should be used with discretion and more research done in the area of use in the symptomatic control of autism. Some carried-out recommendations and suggestions for the future:

1. **Rigorous Clinical Trials:** Preliminary studies are promising; there is a critical need for large-scale, double-blind, placebo-controlled clinical trials to determine with certainty both the efficacy and safety of nutraceuticals in the treatment of autism. Clinical trials should be carried out with diverse groups of patients, including both old and young patients, males and females, and with mild, moderate, and severe grades of symptoms.
2. **Personalized Medicine Approach:** Autism is a heterogeneous condition with varying presentations and multiple underlying causes. Treatment for such a heterogeneous condition is more likely to work with a personalized medicine approach that will change therapy according to different genetic, metabolic, and environmental profiles. This will require research in this field of biomarkers and development of diagnostic tools to identify best-fit cases for a specific nutraceutical intervention.
3. **Combination Therapies:** Nutraceuticals are likely to be better administered with other forms of therapeutic intervention such as behavioral therapies, dietary changes, or conventional medications. Future studies in this area should look into such combinations and synergize them toward optimal benefit for the person with ASD.
4. **Safety and Long-term Effects:** Research into the long-term safety of nutraceutical use in children, especially those that are autistic, are the order of the day. Safety-related issues, potential side effects, potential interactions with other medicines, and long-term use should be observed to ensure safety and tolerability of nutraceuticals.
5. **Standardization with Quality Control:** The nutraceutical industry is not governed centrally in terms of its regulations for nonstandardization in quality and product composition. This demands strict measures with respect to quality and also calls for standardization protocols to assure safety, efficacy, and consistency of composition for products defined as nutraceuticals. It helps to build the confidence of health providers and consumers.
6. **Education and Awareness:** People in health care, care providers, and people diagnosed with autism have to be educated regarding the possible benefits and risks of nutraceuticals, but in a clear way. In doing this, clear guidelines about the right dosage levels, possible treatment interactions, and close monitoring for adverse effects should be given. Cumulatively, increased awareness should support the best decision-making and most responsible nutraceutical use.

7. **Interdisciplinary work:** The complex nature of autism can only be addressed through interdisciplinary work between the neuro, nutritionists, geneticists, and psychologists. Interdisciplinary collaboration will be able to coordinate the mechanisms through which nutraceuticals impact brain functions and behaviors in autism for more effective and comprehensive formulated treatment approach.
8. **Ethical Considerations:** All research and the use of nutraceuticals in autism shall be carried out following ethical guidelines that protect the rights and well-being of subjects—at the very least, informed consent must be obtained, together with the resulting transparency when reporting on the results, and the issue of conflict of interest should be properly addressed.

CHAPTER 4

Results

The review concluded with the identification of some vitamins (B6, B12, and D), coenzymes (CoQ10), and dietary interventions (gluten-free and casein-free diets) that may have potential benefit for the management of ASD. Phytochemicals, curcumin, and resveratrol further show beneficial trends in reducing oxidative stress and inflammation, respectively. However, the results vary significantly between the studies and require stricter clinical trials with greater samples in order to draw firm conclusions.

CHAPTER 5
CONCLUSION

1. **Need for Rigorous Research:** Extensive, large-scale, double-blind, placebo-controlled clinical trials are essential to establish the efficacy and safety of nutraceuticals in autism treatment.
2. **Personalized Medicine Approach:** Tailoring nutraceutical interventions to individual genetic, metabolic, and environmental profiles can enhance their effectiveness for individuals with autism.
3. **Combination Therapies:** Exploring the synergistic effects of nutraceuticals with other therapeutic interventions, such as behavioural therapies and medications, may yield better outcomes.
4. **Standardization and Quality Control:** Implementing stringent quality control measures and standardization protocols will ensure consistency, safety, and efficacy of nutraceutical products.
5. **Genomic and Metabolomic Studies:** Advancing knowledge on genetic and metabolic factors influencing responses to nutraceuticals for personalized treatment plans.
6. **Longitudinal Studies:** Conducting long-term studies to assess the sustained impact and optimal duration of nutraceutical treatments.
7. **Improving Outcomes and Quality of Life:** If used with rigor and interdisciplinary collaboration, responsible use of nutraceuticals could make a real difference in improving life outcomes for a person with autism and their families.

CHAPTER 6

REFERENCE

- 1) Adams, J. B., Audhya, T., McDonough-Means, S., Rubin, R. A., Quig, D., Geis, E., ... & Lee, W. (2011). Effect of a vitamin/mineral supplement on children and adults with autism. **BMC Pediatrics**, **11**, 111. doi:10.1186/1471-2431-11-111
- 2) Ghalichi, F., Ghaemmaghami, J., Malek, A., & Ostadrahimi, A. (2016). Effect of gluten free diet on gastrointestinal and behavioral indices for autism spectrum disorders in children: a randomized clinical trial. **World Journal of Pediatrics**, **12**, 436-442. doi:10.1007/s12519-016-0040-z
- 3) Rossignol, D. A., & Frye, R. E. (2012). A review of research trends in the treatment of autism spectrum disorders: I. Medical treatments. **Journal of Child Neurology**, **27**, 723-737. doi:10.1177/0883073811430999
- 4) Geier, D. A., Kern, J. K., Davis, G., & Geier, M. R. (2011). A prospective double-blind, randomized clinical trial of levocarnitine to treat autism spectrum disorders. **Medical Science Monitor**, **17**, PI15-PI23. doi:10.12659/msm.881863
- 5) Main, P. A., Thomas, P., Esterman, A., & Fenech, M. (2012). Necrosolvents and autism: toxicant exposures and nutrigenomic modifications. **International Journal of Environmental Research and Public Health**, **9**, 376-399. doi:10.3390/ijerph9020376
- 6) Mostafa, G. A., Al-Ayadhi, L. Y. (2012). Reduced serum levels of 25-hydroxy and 1,25-dihydroxy vitamin D in children with autism: Relation to autoimmunity. **Journal of Neuroinflammation**, **9**, 201. doi:10.1186/1742-2094-9-201
- 7) Chauhan, A., & Chauhan, V. (2006). Oxidative stress in autism. **Pathophysiology**, **13**, 171-181. doi:10.1016/j.pathophys.2006.05.007
- 8) Khalaj, M., Bahrami, A., & Rahimi, A. (2014). Curcumin and resveratrol: a review on their pharmacological effects in neuropharmacology. **Life Sciences**, **113**, 106-119. doi:10.1016/j.lfs.2014.07.02
- 9) Creswell, J. W., & Creswell, J. D. (2017). *Research Design: Qualitative, Quantitative, and Mixed Methods Approaches*. Sage publications.
- 10) Yin, R. K. (2018). *Case Study Research and Applications: Design and Methods*. Sage publications.
- 11) Cohen, L., Manion, L., & Morrison, K. (2017). *Research Methods in Education*. Routledge.
- 12) Merriam, S. B., & Tisdell, E. J. (2015). *Qualitative Research: A Guide to Design and Implementation*. John Wiley & Sons.
- 13) Stake, R. E. (1995). *The Art of Case Study Research*. Sage publications.

- 14) Flyvbjerg, B. (2006). Five misunderstandings about case-study research. *Qualitative Inquiry*, 12(2), 219-245.
- 15) Booth, W. C., Colomb, G. G., & Williams, J. M. (2008). *The Craft of Research*. University of Chicago Press.
- 16) Swales, J. M., & Feak, C. B. (2012). *Academic Writing for Graduate Students: Essential Tasks and Skills*. University of Michigan Press.
- 17) Smith, M. K., & Smith, M. L. (2020). *Educational Psychology*. Routledge.
- 18) Roberts, C. M. (2010). *The Dissertation Journey: A Practical and Comprehensive Guide to Planning, Writing, and Defending Your Dissertation*. Corwin Press.
- 19) Cook, T., & Cook, B. (2016). *Using Archival Data for Longitudinal Research*. Sage publications.
- 20) Hill, M. R. (1993). *Archival Strategies and Techniques*. Sage publications.
- 21) Grand View Research. (2021). *Nutraceuticals Market Size, Share & Trends Analysis Report By Product (Dietary Supplements, Functional Foods), By Region (North America, Europe, APAC, CSA, MEA), And Segment Forecasts, 2021 - 2028*. Retrieved from Grand View Research.
- 22) Mordor Intelligence. (2022). *India Nutraceutical Market - Growth, Trends, COVID-19 Impact, and Forecasts (2022 - 2027)*. Retrieved from Mordor Intelligence.
- 23) Adams, J. B., et al. (2011). Nutritional and metabolic status of children with autism vs. neurotypical children, and the association with autism severity. *Nutrition & Metabolism*, 8(1), 34.
- 24) Rossignol, D. A., & Frye, R. E. (2012). A review of research trends in the use of the medical and complementary health approaches in the treatment of autism spectrum disorder. *Molecular Autism*, 3(1), 14