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Does Camel's Milk contain specific Nanoparticles for the treatment of Autism in children? Review Literature

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Abstract

Many research findings investigated that camel's milk is more similar to human milk than the milk of other animal species. It is easily digested by Lactose-intolerant individuals. Camel's milk is rich in minerals like Iron and Vitamins particularly, Vitamins B and C. Moreover, the lactoferrin in the milk of camel has antibacterial, antiviral, and anti-tumor properties. Additionally, camel's milk contains disease-fighting immunoglobulins that are small in size, allowing penetration of antigens and boosting the effectiveness of the immune system. This review of literature intends to focus on the role of camel's milk in the treatment of autism syndrome in children. Scholarly articles as well as search engines were such as Google Scholar, Medline, and EMBASE were consulted to explore the relationship the camel's milk has with autism. The findings of the selected research articles approved that camel's milk could play an important role in decreasing oxidative stress in patients with autism. It can alter antioxidant enzymes and nonenzymatic antioxidant molecules levels that lead to recovery of the autistic behavior, as demonstrated by the improved Childhood Autism Rating Scale (CARS). In conclusion, the study approved that camel's milk can decrease autism syndrome. The authors recommend doing more clinical and analytic research on the therapeutic properties of camel's milk in the treatment of children suffering from autism.

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Introduction

Many scientists have in recent years reported the presence of nanoparticles in camels' milk. These are in turn used for the treatment of many disease conditions and disorders such as autism, diabetic mellitus, cancer and many genetic diseases (AlNohair, 2020).

Autism spectrum disorder (ASD) is a severe disorder of neurological development with an onset that manifests in children before their three years of age (Lord *et al.,* 2000; American Psychiatric Association, 2000). It is characterized by social orientation and communication impairments, and repetitive behaviors (Momeni *et al.,* 2012; Veenstra-Vander and Cook, 2004). Other ASD symptoms in addition to behavioral impairment are that it is linked to the high prevalence of autoimmune diseases (Ashwood**,** et al, 2011 & Al-Ayadhi, and Mostafa**.** 2012), gastrointestinal disease and dysbiosis (White, 2003), and mental retardation (Bölte & Poustka, 2002). Over the last decades, the prevalence of autism has surprising and several research studies revealed that the incidence of ASD in the United States had increased in 2008 to 1 in 88 children (Autism and Developmental Disabilities Monitoring Network Surveillance Year 2008 Principal Investigators. 2012). Another study conducted in Saudi Arabia revealed that the prevalence of the spectrum disorders of autism was in the ratio of 6 in 1000 children (Al-Gadani *et al*., 2009). The increasing ASD prevalence greatly affects the public health and the implications have passionately stimulated researches into potential etiologic factors. Despite the poor understanding of the etiology and pathology of autism, it is suggested that various factors are associated with it such as environmental, immune, genetic and neurochemical factors (Schopler *et al*.,2010), as well as oxidative stress (Castelloe, & Dawson, 1993; Chauhan *et al*., 2004)**.** A study was conducted by Ahmad Ghanizadeh, (2012) in which the neurobiology of autism and the mechanism-based function of gold nanoparticles plus LA (Ghanizadeh, 2012), were considered. This lead to hypothesis that gold nanoparticles plus LA improve the symptoms of autism by enhancing the defense mechanism against oxidative stress (Ghanizadeh, 2012). The study further evaluated the effects of consumption of camel milk on the biomarkers of oxidative stress in children with autism by measuring the glutathione levels in plasma, dismutase, superoxide and myeloperoxidase levels. These levels were examined before and two weeks after the consumption of the camel milk using enzyme-linked immunosorbent assay (ELISA) technique. There was a significant increase in the levels of all the parameters measured after the camel milk was consumed ($P < 0.5$). The findings herein suggested that the milk of camel can play a vital role in decreasing oxidative stress. This is achieved by alteration of the levels of antioxidants enzymes and nonenzymatic antioxidant molecules thereby improving autistic behavior as demonstrated by the improved Childhood Autism Rating Scale (CARS) (Laila *et al*., 2013). Thus, this review aims to focus on the role of nanoparticles of camel's milk in treating autism syndrome in children.

Biotechnology of nanoparticles used in the treatment of autism

Systems of nanoparticles are able to provide a relatively cheap and simple option to prevent maternal-autoantibody-related (MAR) autism. Nanoparticles are composed of various nanostructures that include graphene, gold, silica, and iron that demonstrate extensive applications in targeted drug delivery (Petros & De Simone, 2010). Of these, are iron oxide nanoparticles (IONPs) that emerge as excellent candidates for biomedical applications, basically owing to their desirable physical characteristics such as the high ratio of surface area to volume and inherent magnetism (Stephen *et al.*, 2011). Such qualities have forced the use of IONPs in clinical MRI (magnetic

resonance imaging) as contrast agents and for the separation of environmental contaminants (Wu *et al*., 2015; Tang *et al*; 2018; Tu *et al* ., 2011**;** Banobre-Lopez *et al.,* 2013). Other characteristic advantages of the IONPs include stability, biocompatibility, low cost, and environment-friendliness (Tu *et al* ., 2011). The Food and Drug Administration (FDA) has notably approved IONPs for use as MRI contrast agents and as supplements for iron deficiency (Lu *et al*., 2007).

Autism

Autism refers to the collection of behavioral symptoms with characteristic social interaction and dysfunction of communication observed in affected children. It is usually linked with stereotypic, repetitive and restrictive behavior and displays within the first three years of life. The cause of such disorder is still unknown (Horvath Karoly & Perman Jay 2022), and ought to be investigated as a variant of behavior (Mottron, 2011). However, various factors including environmental, genetic neurological and immunological elements have been implicated in its pathogenesis (Parcell, 2011). Some clinical studies conducted recently have revealed a high prevalence of inflammation, gastrointestinal discomfort, and dysfunction in children suffering from autism. Inflammations of moderate and mild intensities in both the upper and lower intestinal tracts were also found to be associated with autistic children (Horvath Karoly & Perman Jay 2022). It was theoretically conceived by Panksepp (1979) that components of autism may be due to excessive opiate activity (Panksepp , 1979). A hypothesis by Dettmer et al (2007) referred to as ‘opioid peptide excess’ postulated that excessive amounts of endogenous or exogenous opioid peptides derived from dietary proteins from cow milk may be pathophysiologically important in autism (Dettmer *et al.,* 2007). Casein proteins are not completely metabolized in the intestine of ASD subjects. This is due to a deficiency in enzymatic activity which is in turn due to the formation of short neuroactive peptides – such as B-casomorphins derived from casein. B-casomorphin-7(BCM 7) has been regarded as one of the major risk factors for autism. However, there is the controversy behind this hypothesis. Most of autism-affected children suffer from the effects of digestive disorders that make them susceptible to the absorption of BCM7 (Woodford, 2011). Additionally, it has been suggested that BCM-7 is implicated in causing sudden infant death syndrome (SIDS). Moreover, neurological disorders such as schizophrenia and autism are believed to be associated with the consumption of milk and a higher level of BCM-7. Thus, researcher-made awareness about protein polymorphism and deeper research to verify the range and nature of its interactions with the human gastrointestinal tract and whole organism are recommended (Kamiński *et al.,* 2007). Oxidative stress takes place when the levels of reactive oxygen species (ROS) become higher than the cell’s antioxidant capacity. It mediates strokes, brain injury, and neurodegenerative diseases (Shohami *et al.,* 1997; El-Ansary *et al.,* 2010; Zoroglu *et al.,* 2004). Thus for the cell to function physiologically effectively, ROS production control is necessary. The ROS within the cells is usually neutralized by the defense mechanisms of antioxidants, such as catalase, superoxide dismutase (SOD), and glutathione peroxidase (GSH-Px) enzymes. The increased production of ROS both in the brain (centrally) and in the plasma (peripherally) may eventually result in reducing brain cell numbers thereby leading to apoptosis and autism pathology (Christen, 2000; Russo, 2009).

Several research studies conducted have suggested the role of oxidative stress in autism development. Such studies have demonstrated the change of antioxidant enzymes such as GSH-Px, MPO, and SOD, lipid peroxidation, antioxidant proteins such as ceruloplasmin and transferrin, and detoxifying metabolites like GSH and antioxidant nutrients, minerals, and vitamins (Meguid *et al.,* 2011; Chauhan, & Chauhan, 2006).

Camel milk

Camel milk is important to our daily life as a source of food and the camel itself serves as a means of transportation in the desert. Camel milk has also been used as medicine for diverse illnesses since ancient times (Gader, & Alhaider, 2016). Camels are able to produce much more milk for a longer period in arid zones and harsh environments than any other species of domestic livestock (Ahmed, 2011). Camel milk is so-called 'the white gold of the desert and is more similar to human milk than any other milk and differs from other ruminant milk due to its low sugar, low cholesterol, high vitamin C, high minerals (sodium, potassium, iron, copper, zinc, and magnesium), protective proteins such as lysozyme, lactoferrin, immunoglobulins, lactoperoxidase, and lysozyme contents (Yadav *et al.,* 2015). Acknowledging camel milk for the provision of a series of diseases and disorders has been done for a long period of time. These diseases and disorders include hypertension, jaundice, dropsy, leishmaniasis or kala-azar, and asthma (Yadav *et al.,* 2015; Asresie, & Yusuf, 2014). It is a frequent practice in India the use camel milk as traditional medicine owing to its wide applications in the field of biomedicine. It is employed in the treatment of several antimicrobial diseases due to its strong antibacterial contents. It reportedly has a stronger antimicrobial inhibitory effect than that cow milk (Agamy *et al.,* 1992). It is globally accepted that camel milk has proved to be suitable for the production of a variety of derived products with substantial nutritional value (Khalesi *et al.,* 2017). Camel milk components have been described by various research studies attributing it with antiviral and bacteriostatic activities. These have contributed immensely to its activities of protective proteins like lysozymes, immunoglobulins, lactoferrin, and lactoperoxidase (Kappeler, 1998). The presence and high amount of these proteins helps to explain some of its natural healing properties.

Elimination diets of gluten or casein are beneficial to children with ASDS. This has been discussed in numerous publications, books, and parent/lay Autism conferences. Such elimination diets make them less vulnerable to the neuro-active peptides derived from casein/gluten protein. Camel milk is devoid of beta-lactoglobulin found in cow milk and a different beta-casein (Shabo *et al.,* 2005); two of the cow milk components that cause allergies. Additionally, camel milk whey proteins exhibit different electrophoretic behavior than those found in other animal species. Structural variations also exist in the sequence of amino acid ß-casein in the camel with that found in cow milk. This makes camel milk beneficial to subjects with various physical and mental disorders in comparison with that cow milk. Camel milk proved effective in a controlled study amongst a group of children that were believed to have suffered from Autism Spectrum Disorders (ASD).
Camel milk has also emerged to have possible effects of therapy against many disorders such as diabetes mellitus, food allergy (Agrawal *et al.,* 2005), hepatitis B

(Saltanat *et al.,* 2009), autism (Shabo, & Yagil, 2005), and other autoimmune diseases (Yagil, 2004). It has unique compositions that entirely differ from the milk of other ruminants such as low cholesterol, low fat, and lactose in comparison with that of cow milk. It also has higher minerals (magnesium, calcium, iron, copper, potassium, and zinc), and vitamins A, B2, E, and C than cow milk (Mohamed *et al.,* 2005). Camel milk does not contain beta-lactoglobulin and beta-casein which are the main cause of allergy in cow milk (Shabo *et al.,* 2005). Furthermore, camel milk contains various protective proteins, mainly enzymes that are capable of exerting properties that are immunological, antiviral, and antibacterial in nature (Kappeler *et al.,* 1998). These proteins include N-acetyl-§- glucosaminidase (NAGase), lactoferrin, immunoglobulins, lysozymes, lactoperoxidase, and peptidoglycan recognition protein (PGRP) (Shabo *et al.,* 2005); they are of great importance in the prevention of food allergy and in the rehabilitation of the immune system (Yagil, 2004). Camel milk proved its potential effect in the treatment of food allergies, due to its inflammation-inhibiting proteins, and hypoallergenic properties, in addition to its small-sized nanobodies different from those found in humans. Camel milk nanobodies, as a single domain, show many promising and therapeutic potency in immunity and infection (Zafra *et al.,* 2011).

Mechanisms of Camel Milk to Treat Autism

Those who practice therapy using camel milk believe that many autism characteristics are as a result of high levels of reactive oxygen species (ROS). ROS are highly reactive molecules that are naturally found in the cells of the human body. Research studies have found out that high ROS levels may lead to many diseases and disorders such as cancer and autoimmune diseases. Anti-oxidants help to lower ROS levels and these are readily in abundance in camel milk (**S**welum *et al.,* 2021).

Several studies explored camel milk as a potential substrate of protein that generates bioactive protein hydrolysates with antioxidant activities (Al-Saleh *et al.,* 2014; Shori, & Baba, 2014). The study by Salami *et al.,* (2011), and Jrad *et al.,* (2014a) reported an elevation of antioxidant activity of camel milk's casein hydrolysates when digested with gastrointestinal enzymes (Salami *et al.,* 2011; Jrad, *et al.,* 2014). The assays that determine the capacity of the antioxidant are categorized into two groups on the basis of the chemical reactions; the first group includes the methods based on electron transfer (ET), like ferric ion reducing antioxidant power (FRAP) and 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical-scavenging assay (Jrad *et al*., 2014). The second group is based on hydrogen atom transfer (HAT) like oxygen radical absorbance capacity (ORAC) and total radical trapping antioxidant parameter (TRAP) assay (Sarmadi & Ismail, 2010). Several researchers that support the activity of camel milk as a therapy for autism claim that the antioxidants in camel milk can reduce ROS levels in autistic children. This in turn can reduce the characteristics of autism in children (Al-Ayadhi & Elamin 2013), Figure (1) depicts the mechanisms involved in camel milk's ability the treatment of autism.

In conclusion, this review literature shows that camel milk contains specific nanoparticles, bioactive peptides, lactoferrin, zinc, and mono and polyunsaturated fatty acids and antioxidants, with antioxidant, antimicrobial, Angiotensin-Converting Enzyme (ACE) inhibition effects which are all representing the major special mechanisms to cure autism in children.

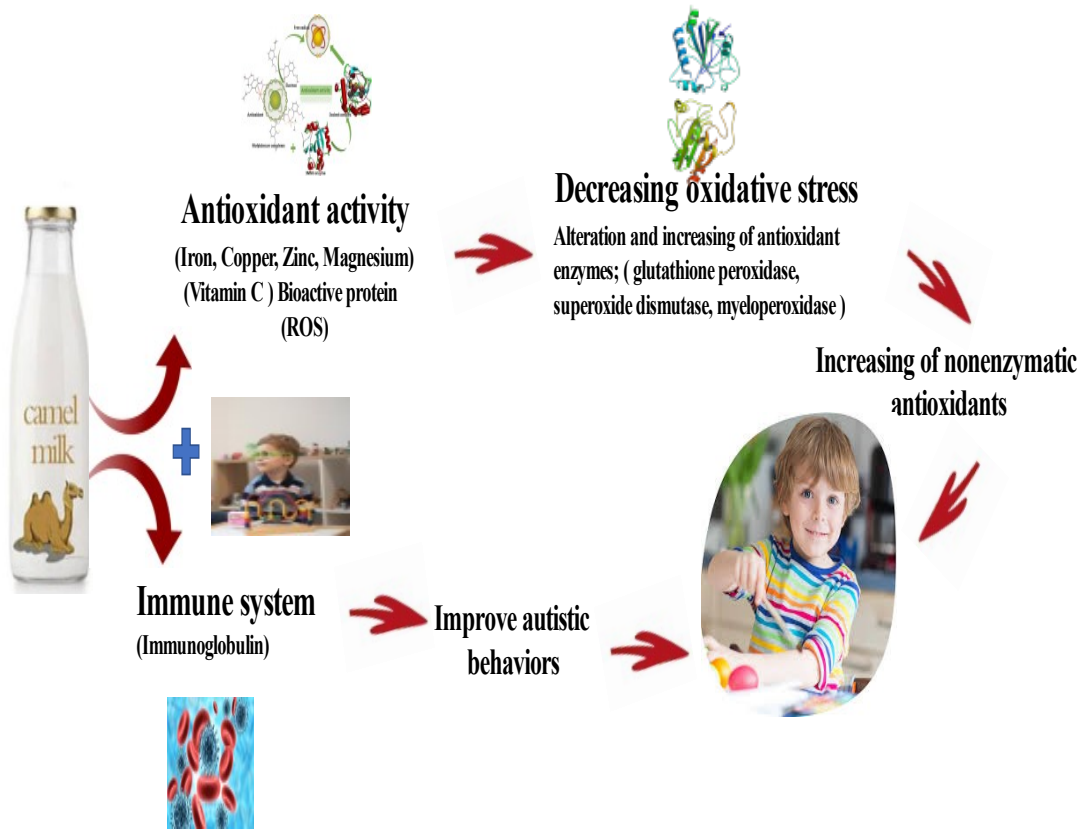

Figure 1. Mechanisms of Camel Milk to Treat Autism

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