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The therapeutic effect of nanoparticles on toxoplasmosis

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ABSTRACT

Background: Toxoplasmosis is a worldwide parasitic disease resulting from the protozoan parasite *Toxoplasma gondii;* an obligatory intracellular parasite that belongs to the phylum Apicomplexa infecting nearly one-third of humans, with possible excessive consequences in neonates and immunocompromised patients. Acute on top of chronic exacerbation of infection is very dangerous when immunity drops. Current treatment programs consist of using conventional chemical compounds or herbal compounds which have restricted entry to the brain, despite their high harmlessness to the host. Enhancements are wished in treatment programs and formulations to deal with those infections and to allow the medication to cross the central nervous system. Different forms of nanomaterials are utilized in nanotechnology and are composed of numerous constituents, involving polymers, lipids, and metals. The reduced size of nanoparticles allows them to enter the blood-brain barrier leading to extra activity. Metal nanoparticles, for example, silver and gold, reveal anti-parasitic activities. **This study aims** to spotlight the therapeutic effect of nanoparticles on toxoplasmosis.

Keywords: Nanoparticles, Toxoplasmosis, Treatment.

Introduction

Toxoplasma gondii is a global parasite belonging to the protozoa that affect a lot of mammals [1]. The parasite shows more than one infective stage, such as bradyzoite, tachyzoite, and sporulated oocyst. Felines, especially cats, are the final hosts of the parasite. Oocysts in cats' stool need about 2 weeks in the atmosphere to become infective sporulated. Infection of intermediate hosts such as man by digestion of sporulated oocysts transforms them into tachyzoites.

An acute phase is considered when tachyzoites replicate quickly by binary fission. Then they invade tissues such as the eye, brain, heart and skeletal muscles, and the placenta. The chronic stage begins when the immune system forms walls surrounding tachyzoites and converts them into tissue cysts that contain bradyzoites. When immunity drops, some bradyzoites are released from tissue cysts and become tachyzoites, which is responsible for acute exacerbation [2].

Toxoplasmosis of men is mostly caused by ingestion of tissue cysts in contaminated undercooked meat and consumption of infected meals with sporulated oocysts [2-3]. Pregnant women that get a primary infection can transmit

tachyzoites through their placenta to the developing fetus. Infection can also arise through blood transfusion or organ transplantation from infected donors [4-5]. Infection is asymptomatic in immunocompetent individuals, but it can be lethal in immunocompromised individuals. [6]

Acute on top of chronic exacerbation of infection is very dangerous when immunity drops [7]. The first organ that can be involved in acute infection is the brain, which may give rise to encephalitis. Multi-organ involvement and acute respiratory failure can also occur. Congenital infection depends on the gestational age at the time of primary maternal infection, which can result in abortion, fetal death, or premature birth, cerebral manifestations include convulsions, intracranial calcifications, hydrocephalus, mental retardation, and ocular manifestations such as chorioretinitis and blindness can also occur [8-9].

Treatment of toxoplasmosis

Treatment of infection is almost considered in the following situations: (1) primary infection in pregnant women to prevent congenital infection; (2) infants with congenital toxoplasmosis; (3) acute exacerbation of infection on top of chronic exacerbation in immunecompromised individuals; and (4) acute chorioretinitis [10]. The parasite is unable to use food folates and it forms folates by itself [11]. Spiramycin, Pyrimethamine sulfadiazine, and pyrimethamine-clindamycin are examples of traditional treatments. [12] These drugs block the formation of parasite folate, thus nucleic acid biosynthesis and parasite replication. But, these drugs have several harmful effects, such as severe thrombocyte-penia [13], a rise in serum creatinine and liver enzymes, and severe allergic manifestations. **These** drugs are usually administered with folinic acid [11].

Pyrimethamine should not be used in the first trimester of pregnancy as it can cause teratogenicity [9].

Spiramycin has been described as safe during the first trimester and it decreases tachyzoite entrance through the placenta [14]. Spiramycin can not enter into the fetus and hence is not dependable for the management of an infected fetus. It is taken till the end of pregnancy due to the hypothetical chance that affection of the fetus can arise at any time during gestation from a previously infected placenta [15].

Nanotechnology and Nanomedicine

With the invention of the scanning tunneling microscope in the early 1980s, nanotechnology and nanoscience were born. This led to the discovery of carbon nanotubes and the manufacturing and characterization of semiconductor nanomaterials [16]. The atomic force microscope is a very high-resolution form of scanning probe microscopy, with an established resolution of elements of a nanometer, over and above 1000 times better than the optical diffusion bound. The slope of the scanning probe can, moreover, be used to employ nanostructures [17].

Nanotechnology is the advancement of technology on the nanometer scale, typically 0.1- 100 nm. A nanometer is one-billionth of a meter that cannot be seen by a traditional microscope. Nanomedicine, an offshoot of nanotechnology, refers to highly definite therapeutic interference on the nanoscale [18]. It utilizes nano-sized devices for disease management [19]. Nanoparticles comprise a variety of ingredients that contain specific substances with one measurement of less than 100 nm [20]. According to the general form, those substances possibly 0, 1, 2, or 3 dimensions [21]. The significance of these substances was discovered when scientists discovered that dimension can

affect a material's physiochemical characteristics [22].

The benefits of these substances arise when they were manufactured utilizing natural biological substances such as vitamins, proteins, lipids, carbohydrates, botanical extracts, biodegradable polymers, and microorganisms. These developments cause the production of a few inorganic nanoparticles, mostly metal nanoparticles, several metal oxides, and salts [23]. Because of their reduced size, they show much greater specific surface area, since the whole surface area of a molecule is contrariwise related to its length [24]. Furthermore, this reduction in size permits a better intake and is more appropriate for drugs used by injection. [25] These substances have dimensions in the same variety of units, directing basic cellular purposes. Furthermore, certain characteristics, such as ocular responses, are size-dependent and only present at the nanoscale, allowing their use in imaging procedures [26].

These substances have distinctive physicochemical characteristics, for example, extreme trivial size, great surface area to mass proportion, and great reactivity, which are unlike bulk constituents of similar structures. These characters can be used to get rid of some restrictions observed in conventional therapeutic methods [27].

Classification of nanoparticles:

Nanoparticles are broadly divided into various categories reliant on their morphology, size, and chemical properties. They are classified into the following groups [28].

(i) Carbon-primarily-manufactured nanoparticles

They were discovered in different morphologies such as hollow tubes, ellipsoids, and spheres. Carbon nanotubes, nanofibers, graphene, and are involved in this group. Laser ablation, arc discharge, and chemical vapor deposition are the important manufacture methods for these materials manufacture [29].

(ii) Inorganic-primarily- manufactured nanoparticles:

They comprise metal and metal oxide nanomaterials that can be manufactured into metals such as gold or silver nanoparticles, metal oxides, and semiconductors as ceramics [30].

(iii) Gold nanoparticles:

These substances are manufactured via the reduction of gold into a fluid phase as it offers the smallest surface area in comparison with other morphologies. Characteristically, the spherical type of these substances presents a dark red color, but the increase in size and the alteration in the environment around them may change their optical characteristics [28].

These substances are present in numerous formulas, like spheres, rods, shells, clusters, and cages for a varied range of uses [31].

Ceramic nanomaterials are inorganic, primarily based molecules manufactured by heating followed by cooling. They can be found in amorphous, polycrystalline, dense, porous, or hollow formulas [32]. These nanoparticles are utilized in applications such as photocatalysis, photodegradation of dyes, and imaging procedures [33].

(iv) Organic- primarily- manufactured nanoparticles:

These substances are made from biological substances. Organic nanomaterials are converted into assemblies such as liposomes and dendrimers through the use of noncovalent interactions and molecule design. [30]

Dendrimers are higher nanomaterials combining several unique characteristics such as (i) hyperbranched and three-dimensional structural engineering; (ii) very good liability and functionality [34].

(v)Composite- primarily manufactured nanomaterials:

These substances may be any mixtures of inorganic, organic, or carbon-primarily based nanomaterials with one ceramic, metal, or polymer constituent. [30]

Nanoparticles have the facility to provide drugs in the best dose that results in the increased therapeutic efficacy of these medications, decreasing side effects, and improving patient compliance [35].

They have improved the drug's bioavailability even in very subtle treatments as in brain infection [36].

The application of antiviral or anti-parasites needs longer dose intervals (continuous release dosage form in therapy or vaccinations) which raises the significance of assessment of different forms of drug delivery against pathogens by nanoscaled particles [37].

A very common and critical problem with antiparasitic medications is the development of pharmaceutical resistance by weak delivery of these medications to infected cells, so parasites have enough time to remove pharmaceutically effective doses at molecular and cellular levels [38]. Nanomaterials provide an effective implementation to eliminate hazards of resistance to medications resulting from efficient cellular uptake and avoiding these mechanisms [39].

Applications of nanomedicine in toxoplasmosis:

Pissuwan *et al.*, (2009) studied the effectiveness of gold nanoparticles conjugated with *anti- Toxoplasma gondii antibodies* for the *antigen* of the acute strain (RH) of this parasite and treated with laser light. They concluded that the death rate of tachyzoites *in vitro* was elevated by dose-dependent levels of gold nanoparticles in a given laser dose, but there was an insignificant change in the death rate when the laser dose was elevated to a fixed concentration of nanomaterials [40].

A study by ***Kunjachan* et al.,** ***(2011)*** evaluated the treatment of infection in experimental animals by using Chitosan and silver nanomaterials and compared using them singly or together. Using them together revealed a significant reduction of parasite load in the liver and spleen. Also, there was an irregularity in the wall of the tachyzoites, and the tachyzoites showed no motility under microscopy [41].

Azami *et al.*, (2018) assessed the therapeutic effect of nanoemulsion of Curcumin in acute and chronic strains of the parasite in mice and found that in acute infection, the survival time of mice infected with an acute strain of the parasite and treated with the emulsion was statistically significantly increased compared with the control group. Moreover, the emulsion significantly reduced the mean counts of tachyzoites in the peritoneum of acutely infected mice in comparison with control nontreated mice [42].

In addition, chronically infected mice treated with the emulsion showed a significant reduction in the mean number and size of tissue cysts in comparison with those in the control nontreated group ($P < 0.001$).

A similar study made by **Alajmi *et al.*, (2019)** found that the management with silver nanomaterials produced by date palm was stronger than standard treatments in preventing toxicity of the liver by improvement in the immune-histological properties of liver infected mice with the parasite [43].

Another study by **El-Shafey *et al.*, (2020)** showed that Curcumin and Curcumin were incorporated in metal-organic frameworks used in the treatment of infected rats with the chronic ME49 strain of the parasite significantly reduced the mean number of the

parasite cysts in the brains of these rats [44].

Summary and Conclusion

Toxoplasma gondii is an opportunistic parasite that particularly affects immunocompromised persons.

Increased side effects and insufficient proficiencies of medications, particularly against chronic ME49 strain of the parasite, require further work for harmless and effective therapeutic agents.

Nanotechnology refers to technological advances on the nanometer scale. Nanomaterials have sole physicochemical characteristics includes extremely trivial size, great surface area to mass ratio, and extraordinary activity. They have enhanced bioavailability and drug delivery.

Recommendations: Further studies should be done on experimental animals to assess the safety of nanoparticles and avoid toxic doses.

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