Nanotechnology-BasedManagement of Beta-Thalassemia: Exploring Curcumin as a Promising TherapeuticAgent

Abstract

Background: Beta thalassemia is a group of inherited blood disorders characterized by decreased Hb production, which leads to anaemia, and the body does not have healthy RBCs. Individuals need regular blood transfusions. Thus, transfusions frequently result in side effects, including iron toxicity. A polyphenol called curcumin has anti-inflammatory effects and can raise the body's level of antioxidants. The use of nanocurcumin has shown a better treatment option for beta-thalassemia conditions.

Objective: To evaluatethebettertreatment option for beta thalassemia using nano curcumin as a therapeutic tool.

Method:A comprehensive search to identify the relevant studies was conducted in online databases, mainly Google Scholar, PubMed, Embase, and Scopus. Around 100 articles were identified, and after the title and abstract review, 23 students were included in the review. A literature search was conducted to gather information on beta-thalassemia, nanotechnology, and curcumin. Peer-reviewed articles, scientific journals, and relevant databases were utilised to identify relevant studies and research findings. The search was focused on studies that investigated the application of nanotechnology in beta-thalassemia management and the potential benefits of curcumin in this context.

Result: Nanotechnology offers promising strategies for beta-thalassemia management, enhancing drug delivery and gene therapy. Curcumin, with its antioxidant and anti-inflammatory properties, is being explored for beta-thalassemia but faces bioavailability challenges. Strategies like nanoformulations are being investigated for curcumin's delivery.

Conclusion: Nanotechnology-baseddiagnostics, includingnonsenses and nano-biosensors, holdpromise for early detection and monitoring of beta-thalassemia. Curcumin mitigate oxidative stress, reduce inflammation, and potentially alleviate the damage to beta-thalamic RBCs. However, the bioavailability of curcumin remains a challenge, and strategies to enhance its delivery and stability need to be investigated.

Keywords: Betathalassemia, curcumin, nanotechnology.

Introduction:

Beta-thalassemia is a blood disorder that affects the production of hemoglobin, the protein responsible for transporting oxygen throughout the body. It is caused by a mutation in the gene that controls the production of hemoglobin beta globin chains. Beta-thalassemia causes decreased or no beta-globin production, resulting in a deficiency of alpha and beta-globin chains followed by the formation of abnormal red blood cells (RBCs). The severity of beta-thalassemia can range from mild symptoms to life-threatening complications due to genetic mutation. This disease usually occurs in people of Mediterranean, Middle Eastern and Asian descent. [1]

Treatment for beta-thalassemia usually includes regular blood transfusions and iron chelation therapy to control excess iron from the transplant. Continuing research aims to develop new methods, such as nanotechnology-based interventions, to improve the management and treatment of beta-thalassemia.

Nanotechnology plays an important role in the management of beta-thalassemia by providing new solutions in drug delivery, gene therapy and diagnostics. Nanoscale drug delivery, such as nanoparticles and liposomes, improves the targeted delivery of medicinal drugs, increases efficacy and reduces side effects. Nanoparticles can also be used as a delivery vehicle for gene therapy that deliver copies of the beta globin gene or modulate gene expression to restore the balance between alpha and beta globin chains. [2] Nanotechnology-based diagnostic tools such as nanosensors and nanobiosensors enable early and accurate detection of β-thalassemia biomarkers and help monitor disease progression and treatment response. In addition, nanotechnology facilitates the development of iron chelation to control excess iron through regular blood transfusions. Overall, nanotechnology offers promising strategies to improve the management and treatment of β-thalassemia. [2]

Curcumin, a natural compound found in turmeric, has been studied for its therapeutic potential for many diseases such as beta-thalassemia. [3]. Some studies suggest that curcumin may have beneficial effects on red blood cells beta-thalassemia, including antioxidant and anti-inflammatory properties. Beta-thalassemia is associated with oxidative stress and inflammation, which can increase red blood cells. The antioxidant properties of curcumin may help reduce oxidative stress and reduce damage caused by reactive oxygen species. Additionally, curcumin has been shown to have anti-inflammatory properties and can reduce inflammation that damages red blood cells. [4]

In some studies curcumin has been reported to have potential iron chelating properties. In beta-thalassemia, frequent blood transfusions can cause excess iron, which can lead to further complications. Curcumin's ability to chelate iron may help reduce iron overload and its associated effects. [4, 5]

However, it is worth noting that curcumin has a low bioavailability and is rapidly metabolized and excreted from the body. Researchers have explored many strategies to increase the bioavailability of curcumin, such as combining it with other compounds or using nanoparticle delivery systems.

Curcumin

Curcumin, also known as 1, 7-bis(4-hydroxy-3-methoxyphenyl)-1, 6-heptadiene-3, 5-dione, is a lipophilic compound with rapid cell membrane permeability. It is the main ingredient of Curcuma longa L. (commonly known as turmeric) and is found in many forms in plant extracts. [6].

For centuries, turmeric has been used in medicine in China, India and Iran in the treatment of many diseases such as diabetes, liver disease, rheumatoid arthritis, atherosclerosis, infectious diseases and cancer, in the treatment of indigestion, indigestion, bloating, stomach ulcers, blood and stomach pains, duodenal ulcer. Its therapeutic effect on many diseases has attracted extensive research. More importantly, curcumin has been shown in many studies to have antioxidant, anti-inflammatory, apoptosis-inducing and anti-angiogenic properties. It exerts its effects by modulating many targets in cellular pathways, allowing it to exert many therapeutic effects. [7, 8]

Given curcumin's poor bioavailability and selectivity, researchers have introduced and tested numerous analogues of this compound to evaluate their activities against known biological targets and improve their bioavailability, selectivity, and stability. Additionally, several strategies have been introduced to enhance curcumin's bioavailability, increase plasma concentration, and improve cellular permeability while also increasing resistance to metabolic processes. [9]

Among thesestrategies, theuse of nanoparticles for targeted drug delivery has shown promise. Nanoparticles providecurcumin with prolonged circulation, improvedpermeability, and enhancedresistance to metabolicprocesses. This approach offers advantages such as longer retention in the body, increased concentration at the target site, and protection against premature degradation or elimination. [11, 12]

Themechanism of curcumin's action on beta-thalassemiacells

A study conducted by Banerjee, S. et. al showed various effect of curcumin on betathalassemiacells mainly.

1. Anti-Inflammatory Effects: Beta-thalassemia is associated with chronic inflammation due to ineffectiveerythropoiesis and hemolysis, leading to therelease of pro-inflammatory cytokines and mediators. Curcuminexerts its anti-inflammatory effects through multiplemechanisms:

a. Inhibition of NF-κB: Curcumin blocks the activation of nuclear factor-kappa B (NF-κB), a key transcription factor that regulatestheexpression of inflammatory genes. By doing so, curcuminreducesthe production of pro-inflammatory cytokineslike interleukin-1β (IL-1β), tumor necrosis factor-alpha (TNF-α), and interleukin-6 (IL-6).

b. Modulation of MAPK Pathway: Curcumin can interfere with themitogen-activatedproteinkinase (MAPK) signaling pathway, which regulates various cellularresponses, including inflammation. By inhibiting MAPK signaling, curcumindampensthe inflammatory cascade.

c. Suppression of COX-2 and iNOS: Curcumindownregulatestheexpression of cyclooxygenase-2 (COX-2) and inducible nitric oxidesynthase (iNOS), enzymesinvolved in the production of inflammatory prostaglandins and nitric oxide, respectively.

2. Antioxidant Effects: In beta-thalassemia, there is an imbalancebetweenreactiveoxygenspecies (ROS) production and antioxidant defensemechanisms, leading to oxidativestress. Curcumin acts as a potent antioxidant to counteractoxidativedamage:

a. Scavenging of ROS: Curcuminpossessesfree radical scavengingproperties, neutralizing harmful ROS and preventingoxidativedamage to cellularcomponents.

b. Upregulation of Antioxidant Enzymes: Curcumin can upregulateendogenous antioxidant enzymes, such as superoxidedismutase (SOD), catalase, and glutathioneperoxidase, enhancingthecellulardefense against oxidativestress.

c. MetalChelation: Curcumin can chelate transition metals, such as iron and copper, which catalyzethe formation of ROS. By sequesteringthesemetals, curcuminreducestheir participation in oxidativereactions.

3. Iron-ChelatingEffects: In beta-thalassemia, excessive iron absorption and ineffectiveerythropoiesiscontribute to iron overload. Curcuminexhibits iron-chelatingproperties that help in reducing iron burden by:

a. Iron Chelation: Curcumin can form stablecomplexes with iron ions, promoting theirexcretion and limiting iron toxicity.

b. Downregulation of Iron Transporters: Curcumin can decreasetheexpression of iron transporters, such as divalentmetaltransporter 1 (DMT1) and transferrinreceptor 1 (TfR1), reducing iron uptake by cells.

4. Induction of FetalHemoglobin (HbF) Expression: Fetalhemoglobin (HbF) production in beta-thalassemiapatients can amelioratetheseverity of thedisease. Curcumin has been shown to induceHbFexpression through the activation of γ-globin gene transcription, offering a potentialtherapeuticstrategy.

Overall, curcumin's multi-facetedproperties, including its anti-inflammatory, antioxidant, and iron-chelatingeffects, make it a promising therapeuticagent for beta-thalassemia. By targeting various pathological pathways, curcumin has thepotential to mitigateoxidativestress, inflammation, and iron overload in beta-thalassemiacells, ultimately improving diseaseoutcomes. [4, 35]

Curcumin Nanotechnology Approaches:

Nanotechnology has gained significant recognition as a transformative technology with vast potential for the future. One area where nanotechnology holds immense promise is in the field of drug delivery, specifically through the utilization of nanoparticles. These nanoparticles offer exciting opportunities to enhance the bioavailability and solubility of lipophilic compounds like curcumin. [13]

Various types of nanoparticles, such as liposomes, polymeric nanoparticles, micelles, nanogels, niosomes, cyclodextrins, dendrimers, silvers, and solid lipids, have emerged as promising alternatives for delivering curcumin at therapeutic concentrations. [13] These nanoparticles have shown potential in addressing major challenges associated with curcumin, including low solubility, instability, poor bioavailability, and rapid metabolism. They have demonstrated efficacy in diverse applications such as cancer treatment, wound healing, Alzheimer's disease, epilepticus, ischemic diseases, inflammatory diseases. [31]

Isacchi et al. studied and reported the therapeutic benefits of artemisinin or novel liposomal compounds based on a combination of artemisinin and curcumin. They reported that only 7 days after the start of treatment with artemisinin alone, it began to reduce parasitemia and changed the blood affected by the antibiotic. In contrast, treatment of artemisinin loaded with the liposomal delivery system appears to have an immediate antimalarial effect, treating all malaria simultaneously after vaccination. In particular, artemisinin loaded with liposomal curcumin appeared to have the most definitive and potent therapeutic effect in a mouse model of malaria. [22]

The improved blood circulation of artemisinin loaded with liposomal curcumin suggests that these nanosystems could be used as viable vehicles for parasites. This potent formulation adds to the mechanism of action of artemisinin, which acts as a blood-separating agent during the human host's erythroid cycle phase. Agarwal et al. also evaluated the acute effects of liposome-encapsulated curcumin on enhanced current electroshock seizures, pentylenetetrazole-induced seizures, and status epilepticus in rats. Liposome-encapsulated curcumin increased seizure current and myoclonus, and most seizure delays in shock current and pentylenetetrazole-induced seizures, respectively. [22, 23]

Nanotechnology and beta thalassemia

Numerous studies have explored the potential of nanotechnology as a tool to manage beta-thalassemia, a genetic disorder characterized by abnormal hemoglobin production. One notable study by A. K.Singhet al.[24] investigated the use of curcumin-coated nanoparticles, specifically designed to deliver curcumin to the bone marrow. This targeted delivery system has shown promising results by increasing hemoglobin production, which addresses the underlying cause of beta-thalassemia. [24, 25]

Another research effort focused on the use of nanoparticles as carriers for deferiprone, a drug used to treat iron overload associated with beta-thalassemia. Compared to traditional methods, these nanoparticles have shown superior efficacy in delivering deferiprone. In addition, they showed a reduced incidence of side effects, making them a potentially safer and more effective treatment option. [26],

These studies shed light on the potential of nanotechnology in the treatment of beta-thalassemia. By using nanoparticles as transport vehicles, targeted delivery of drugs to affected tissues or cells is possible, which improves treatment results. However, it is important to emphasize that further research is needed to validate these initial findings and expand the range of drugs that can be delivered using nanoparticles to specific cells involved in beta-thalassemia. [25,26]

Onemore study concluded that theeffect of curcumin on beta cells as Curcumin contains multiple functional groups, including phenolic hydroxyl and carbonyl groups, which enable it to chelate metal ions such as iron. In the presence of iron ions (Fe2+ or Fe3+), curcumin forms coordination bonds with iron, leading to the formation of a curcumin-iron complex and the functional groups in curcumin, particularly the phenolic hydroxyl groups, can coordinate with iron ions by donating electron pairs. This coordination involves the formation of bonds between the oxygen atoms of curcumin and the iron ion. The curcumin-iron complex stabilizes through chelation, forming a stable coordination compound. This complexation prevents the release of iron ions and hinders their participation in oxidative reactions, reducing the potential for iron-mediated damage. [25,27]

Reduction of Free Iron: By forming stable complexes with iron, curcumin reduces the pool of free iron available for harmful reactions. Free iron can catalyze the production of reactive oxygen species (ROS) through Fenton and Haber-Weiss reactions, leading to oxidative stress and tissue damage. Curcumin's iron-chelating ability helps minimize these detrimental effects. Curcumin has been shown to facilitate the excretion of iron from cells and tissues. By chelating iron, curcumin promotes its removal through various pathways, including enhanced iron transporters and iron export systems.

Overall, the iron chelation mechanism of curcumin involves its ability to bind to iron ions, forming stable complexes and reducing the availability of free iron. This process helps mitigate iron-mediated oxidative damage and contributes to curcumin's potential therapeutic effects in conditions characterized by iron overload, such as beta-thalassemia. [36]

Application of Nano-curcumin:

Nano-curcumin is a form of curcumin that has been encapsulated in nanoparticles. This makes it more bioavailable, meaning that it can be absorbed more easily by the body. Curcumin is a natural compound that has antioxidant, anti-inflammatory, and anti-cancer properties. It has also been shown to be effective in treating a variety of other conditions, including arthritis, Alzheimer's disease, and cancer. [29]

In recent years, there has been growing interest in the potential use of nano-curcumin to treat beta-thalassemia. There is no cure for beta-thalassemia, but there are treatments that can help to manage the condition. These treatments include blood transfusions, iron chelation therapy, and bone marrow transplantation. However, these treatments can have side effects, and they do not cure the underlying condition. [32]

Nano-curcumin has been shown to be effective in improving the production of hemoglobin in beta-thalassemia patients. In one study, patients who received nano-curcumin showed a significant improvement in their hemoglobin levels, compared to patients who received a placebo. Nano-curcumin was also shown to be safe and well-tolerated by patients. These findings suggest that nano-curcumin may be a promising new treatment for beta-thalassemia. However, more research is needed to confirm these findings and to determine the long-term safety and efficacy of nano-curcumin in the treatment of beta-thalassemia.

Some of the potential benefits of using nano-curcumin to treat beta-thalassemia:

•Nano-curcumin is more bioavailable than curcumin, meaning that it can be absorbed more easily by the body. This could lead to better efficacy and fewer side effects.

•Nano-curcumin can target specific cells, such as red blood cells. This could improve the delivery of curcumin to the cells that need it most.

•Nano-curcumin is a safe and well-tolerated compound. This could make it a more attractive option for patients than other treatments for beta-thalassemia, such as blood transfusions and iron chelation therapy. [33, 34]

Results:

Nanotechnology offers promising strategies for beta-thalassemia management. Nano-sized drug delivery systems, such as nanoparticles and liposomes, provide enhanced delivery of therapeutic agents, improving their bioavailability and reducing side effects. Gene therapy using nanoparticles as carriers has shown potential for delivering healthy copies of the beta-globin gene and modulating gene expression. Nanotechnology-based diagnostics, including nanosensors and nano-biosensors, hold promise for early detection and monitoring of beta-thalassemia.

Curcumin, as a natural compound with antioxidant, anti-inflammatory, and potential iron-chelating properties, has been explored in the context of beta-thalassemia. Studies suggest that curcumin may mitigate oxidative stress, reduce inflammation, and potentially alleviate the damage to beta-thalamic RBCs. However, the bioavailability of curcumin remains a challenge, and strategies to enhance its delivery and stability are being investigated, such as nanoformulations and combination therapies.

Conclusion:

Nanotechnology approaches, including drug delivery, gene therapy, and diagnostics, hold promise for managing beta-thalassemia. Curcumin is a potential complementary treatment. To optimize nanotechnology's potential, we need to develop more stable, bioavailable, and biocompatible nanoparticles through surface modifications. Additionally, rigorous preclinical studies and clinical trials are essential to assess the safety and efficacy of these interventions for individuals with beta-thalassemia.

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