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Review Article

BERBERINE: A POTENT ADJUVANT IN PSORIASIS NANOTECHNOLOGY

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ABSTRACT

Psoriasis is a multi-factorial disease represented by complex atomic scenes and cellular pathways that lead to abnormal cell development. The normal mixture has a clear target and limited cytotoxicity; in this sense, it can support the further development of new therapies for the treatment of this flexible disease. Berberine is an individual of the original berberine alkaloid family. It mainly exists in the roots, trunks and barks of various trees and has anti-psoriatic activity. In any case, according to the berberine organization, limited bioavailability and low assimilation rate are the two main obstacles, because only 0.5% of the ingested berberine is consumed in the small digestive tract, and this rate is when it enters the intestines. It is further reduced to 0.35%. Nano-based details are seen as the best way to increase the assimilation rate because substances accumulated at the nano-level can be quickly absorbed in the intestine. Useful methods based on nanotechnology have been developed to solve these problems to ultimately achieve greater sufficiency in the treatment of various diseases. The investigation introduced and essentially examined the anti-proliferative effects of berberine and nanotechnology-based repair technology for nano-scale transportation of berberine. Finally, we will thoroughly analyze and examine the current methods and promising viewpoints of the recent transportation of this alkaloid.

Keywords: Psoriasis, Berberine, Nanotechnology

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INTRODUCTION

A hundred years of history Psoriasis is a complex disease that is arranged through the multiple cell cycle and palliative changes [1]. The restorative alternatives currently available for the treatment of psoriasis are considered a global health problem and are surprisingly fatal and will promote organ failure, thereby reducing the future, and the cost is very high. Conventional trace elements, such as phytochemicals, have become potential chemoprevention experts, preparing to reduce the risk of disease outbreaks, metastasis, infiltration, and disease transmission [2].

Strangely, more and more evidence shows that phytochemicals have a similar mode of action to conventional chemotherapies. Therefore, unlike traditional self-infection treatments, phytochemicals can be regarded as adjuvant and therapeutic options [3].

Daily use of natural products, vegetables, plants and homegrown products can reduce the risk of some persistent diseases, such as diabetes (DM), cardiovascular (CV) and metabolic diseases, And even psoriasis [4]. Since herbal products are rich in phytochemicals, they promote health and prevent disease [5].

Psoriasis is considered the deadliest infection in the world. Many anti-psoriatic drugs are being developed in clinical and pre-clinical preparations to overcome carcinogenic effects. Both normal (heterocyclic units) and manufactured products (Vinblastine and Vincristine) are also used to combat the expected psoriasis connections and can reduce the proliferation of contaminated cells, thereby increasing patient stability [6]. The nano enemy of psoriasis drugs has become the focus of the world academia because of its designated transport vehicle. Even in the early stages, nano prescriptions can treat psoriasis with minimal side effects. By understanding the specific mode of action of these drugs, these accidental effects can be eliminated [7]. It can be seen that the combination of curcumin ligand and ruthenium particles is less toxic to red blood cells than the currently used manufactured heterocyclic drugs. This metal complex next to the ligand is a potential enemy of psoriasis against HeLa, Hep G2, MDAMB231, and HT29 cell lines [8]. Imidazole is also described as the enemy of psoriasis experts. It is not only an alkaloid and aromatic diazole, but also because it is the human enemy of psoriasis treatment instrument, it is also the height of the psoriasis spectrum [9]. The enemy platinum compounds are also regarded as an important core element in the future treatment of psoriasis. Although these mixtures are considered to have certain limitations, platinum-based co-production can reduce these obstacles. The platinum analogs (lobaplatin, heptalotine) of the third age are more common than the second analogs (carboplatin, oxaliplatin, nedaplatin) [10] because they are more common for psoriasis exercise Good enemy. Certain drugs, such as salicin, naproxen, and diclofenac, can be used to reduce the irritation rate caused by psoriasis. Each of these enemies of psoriasis drugs can be determined by specific chromatographic techniques, such as conversion liquid chromatography (RP-HPLC) and micro-HPLC [11].

Berberise asiatica, belongs to the family Berberidiacae, is a well-known shrub of Garhwal Himalaya and regionally known as "Kingor". In Ayurvedic medicinal system, it is named as 'Daruharidra" or 'Wood Turmeric' due to its similar properties as of turmeric. The plant yields fairly large quantity of alkaloids in which isoquinoline type alkaloids like berberine, palmatine, jetrorrhizine, and columbamine are the most studied phytoconstituents. Berberine is an isoquinoline secondary alkaloid, usually obtained from the roots, stems, barks and rhizomes of Berberis Phellodendron, Coptis, and Coptiscanadensis [12, 13]. Berberine can also be isolated from seeds of Argemone mexicana, which grows as weeds on roadsides and cultivation fields in the temperate regions of India.

Search criteria

This review was made after reviewing approx 200 articles from 2001 to 2021, which were found on electronic database systems like PubMed, Science Direct, and Google Scholar by using keywords like Psoriasis, Berberine, Nanotechnology and their Applications, Pharmacology, and Side effects of berberine, different nanocarriers of berberine, Limitation of berberine etc. After analyzing all articles, few articles were found to be effective for the study about Berberine. Then, a comparative study is presented in this review to make it more informative and relevant.

Limitations of berberine usage

According to records, only 0.5% of berberine intake is in the small intestine Absorption, and when it enters the systemic circulation, this percentage will be further reduced. Various clinical studies

noted that to use as an emulsifier enhancer to increase the absorption rate of berberine by the human body to maximize its clinical effects. Various FDA-approved food additives, including TPGS, Quillaja extract etc have been observed in clinical trials, but it is believed that nano-formulations make an ideal candidate to absorption [14].

Chemistry

Berberine, the most specific isoquinoline alkaloid Berberine (fig. 1) is a member of an alkaloid belonging to the proberberine family. The most common members of this family are leprosy root, Columbamin, Palmatin, berberine, Lambertin, Canadin, and others [15] of Berberine meters The main source of meters contains Barberry (*Berberisspecies*), MeadowRuta (*Thaliceps Species*), Celandine (*Chelidonium species*)), Turmeric (*Coptis spp.),* and Phellodendrongenus. Berberine is mainly separated by alcohol extraction is from after alcohol extraction, is 4 hydrogen chloride, 44 hydrogen chloride salt iodide berberine or dihydrodeoxy berberine [16].

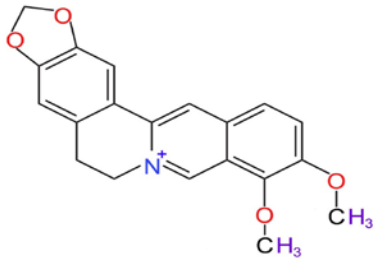

Fig. 1: Chemical structure of berberine [11]

Protoberberine alkaloids are widely recognized for their antibacterial, anti-inflammatory, and anti-oxidant effects [17]. Specifically, *Berberis* (Barberry) Plants of the genus are related to the traditional Japanese medicine used to treat cholera and diarrhea and also used in Indian folk medicine for the treatment of cholera, malaria and other gastric diseases [53]. Several other reports have also shown that barberry can prevent metrorrhagia, renal bleeding and lower blood pressure and is also widely used to treat stomach problems [18].

Pharmacology of berberine

Absorption

The oral bioavailability of berberine is extremely low. Berberine seems to be affected by PG-glycoprotein-mediated efflux from the intestine and liver. In the intestine, PG-glycoprotein is responsible for reducing the transport of berberine by 90%, which pushes berberine back into the intestine. However, when taken together with PG-glycoprotein inhibitors such as cyclosporin A and verapamil, absorption will be greatly increased [19].

Distribution

Animal studies have shown that berberine has a higher tissue distribution after oral administration. It is rapidly distributed to the liver, kidney, heart, brain, lung, muscle, pancreas, and fat and there are no human studies on the distribution of berberine [20].

Metabolism

The liver is the main place for the metabolism of berberine in rats and humans. CYP2D6 is the main human cytochrome P450 producing berberine metabolites, followed by CYP1A2, 3A4, 2E1 and CYP2C19. CYP2D6 plays an important role in berberine metabolism because it is responsible for 9% of the berberine metabolite berberine (M1) and 8% of Thalifendine (M2). The pharmacokinetics and drug interactions of CYP2D6 should be considered when using berberine. After demethylation in phase I, the berberine metabolites of M1 and M2 combine with glucuronic acid and sulfuric acid to form phase II metabolites. Both M1 and M2 can be glucuronated by UGT2B1 and UGT1A1. These glucuronic acid metabolites are polar and are easily excreted [20].

Excretion

There are no human studies on the excretion of berberine. In animal studies on rats, the overall recovery rate of berberine was 22.83% [20]. The main pathway of berberine metabolites is the active ingredient that represents the biological activity of berberine in the body [21]. Similar to the biological activity of berberine metabolites, berberine and its excretion from berberine are feces; the main metabolites of berberine, such as thalifendine (M1), berberine (M2) are mainly passed through bile and urine excretion.

Fig. 2: Pharmacology of Berberine [19]

Berberine as anti-psoriatic drug

Berberine has become an effective antipsoriatic drug over the years [22, 23]. Berberine has a huge antioxidant effect and is suitable for the treatment of various diseases, such as diabetes, diarrhea, and hormone disorders [24]. However, the pro-apoptotic effect of this alkaloid is terrible. Berberine inhibits the proliferation and metastasis of a variety of psoriasis, such as leukemia, colorectal, prostate, lung, glioma and ovarian psoriasis [25-29], although there are certain obstacles that greatly affect the anti-infective properties of berberine. The main reason for this limited apoptotic effect is its poor absorption and limited biological activity. However, with the advancement of nanotechnology, these problems can be overcome [30].

Nanotechnology applied to berberine: an overview

Nanotechnology and nanomedicine have been widely accepted by the scientific community for berberine, which needs to biological ingredients and berberine to reach the formula get the most benefit from traditional therapies. The therapeutic effects of a molecule are directly proportional to the solubility of and are used in pharmaceutical industry. Solubility is one of the key factors that can affect the pharmacokinetics of drugs is approaching to solve the problem of, is "particle-size-reduction", of which drug will be released. The bottom-up and top-down methods has been widely used in the pharmaceutical industry. Nanomaterials are synthesized by physical, chemical, and biological methods or a combination of all methods [54].

Berberine loaded solid nanoparticles

Folic acid-modified chitosan nanoparticles loaded with berberine hydrochloride (BH/FACTS-NPs) are synthesized using ionic cross-linking technology. These nanocomposites have become new players in the treatment of psoriasis by regulating apoptosis and inhibiting the migration and proliferation of Cello saurus cell line 1 (CNE1) cells. Lyotropic liquid crystal nanoparticles (LCN) were used by researchers to infect area psoriasis progress and to increase the solubility of berberine. LCNs nanoparticles are synthesized by an ultra-hygienic method using monoolein, PEG, poloxamer and Transcutol. LCN has been described as a potential active ingredient [31].

Magnetic nanoparticles as berberine nanocarriers

Magnetic nanoparticles promise targeted and controlled drug delivery systems under the influence of a magnetic field. According to reports, iron oxide nanomaterials with different formulations can improve the effectiveness of drugs and control the progression of psoriasis cells in model organisms. Iron oxide nanoparticles are considered an ideal candidate site-specific active ingredient delivery system. By injecting iron oxide nanoparticles and berberine complex (Fe OBBR) into the hind legs of solid-infected mice, a joint study of the resolution of the infection was carried out. Oral Fe OBBR complex in different models, field orientation through magnetic, proof to become. The biological process of apoptosis, Histopathological studies has shown that these biocompatible nano-drug complexes have no effect on surrounding normal cells [32]. Drug-loaded magnetic nanoparticles produced by the co-precipitation method solve Prostatic psoriasis DU145 4 Cell 4 Anti-psoriatic drugs and magnetic particles found in Co-delivery of inhibit the proliferation of psoriasis cells. Gene expression analysis by comet assay and QRT-PCR established a molecular relationship consisting of changes in Baxand bcl expression levels and the triggering caspase activity that induces apoptosis [32, 33].

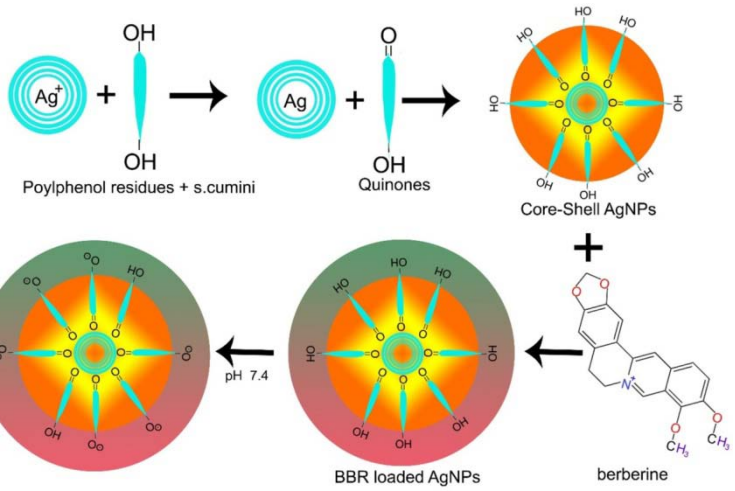

Fig. 3: Synthesis of berberine loaded silver nanoparticles [53]

Silver nanoparticles as berberine nanocarriers

Silver nanoparticles are also used as a transporter for berberine to its destination. Later data confirmed that the anti-psoriatic effect of berberine is more dangerous. It can down-regulate adenosine phosphate-activated protein kinase (AMPK) and hypoxia-inducible factor 1α (HIF1α), limit cell expansion, accept apoptosis, and detect angiogenesis and the development of confusion [34]. In addition, for the MCF 7 cell line, which is usually concentrated on cell lines, it is believed that they are more sensitive to berberine-stacked silver nanoparticles. Therefore, in a xenograft mouse model, berberine-stacked silver nanoparticles can reduce the size and weight of the disease by limiting the proliferation of MCF7 cells without reducing the bodyweight of the mouse model [35]. In addition, in a mouse model of psoriasis in a contaminated area, agNP stacked with berberine has the opportunity to effectively penetrate the cytoplasm of psoriasis cells in the contaminated area and break it down to transport its substances, namely nanoparticles and Berberine, which triggers corresponding cytotoxic effects and induces apoptosis, inhibits the expression of HIF1α by restricting the expression of PI3K/AKT and Ras/Raf/ERK proteins in the marker signaling pathway and ROS individual formation [36].

Chitosan-based nanoparticles as berberine nanocarriers

Chitosan-based nanoparticles are also used as transport carriers for berberine to attack diseased cells because they can further improve the bioavailability of berberine. It is believed that berberine hydrochloride stacked chitosan-based nanoparticles trigger apoptosis in nasopharyngeal carcinoma epithelioid cell line (CNE1) via the FR sinterceded endocytic pathway [33]. Doxorubicin is acutting-edge enemy psoriasis anti-infective agent with atomic DNA embedding capabilities recommended by the US Food and Drug Administration (FDA) for the multi-drug anti-psoriatic treatment under the PEG Liposomal plan (Doxil). In order to improve the viability and cell porosity of doxorubicin, doxstacked nanocarriers have been regarded as one of the most encouraging technologies to inhibit the movement of psoriasis cells [38]. Mitochondria focus on nano-drug transport; experts are said to attack the mitochondrial layer of psoriasis cells by exploiting the increased mitochondrial membrane capacity of psoriasis cells [38, 39]. Subsequent studies have shown that berberine interferes with the use and improvement of mitochondria, focusing on various *in vitro*, *in vivo* and *in vitro* nano-delivery frameworks for drug-safe psoriasis cells. Include doxorubicin to reduce uncontrolled cell growth. One of the illustrative models comes from studies that increase the uptake of doxorubicin; currently, such studies believe that alkylated berberine is the mitochondrial concentration of the ligand, but it is an appendage of alkylated berberine that occurs on C9Changed [39, 40].

DNA nano-bio sensors to determine the effect of berberine on psoriasis cells

Multi-faceted nano-membrane is increasingly recognized as an ideal way to control and target the arrival of antipsoriatic drugs. The programmable 3D DNA origami structure is planned using layered proof technology. They have a unique and practical nano-size surface technology and have been shown to have a significant impact on increasing drug delivery characteristics [41].

Nano biosensor has been used in early detection of different genetic, psoriasis, harmful disease. They are considered a fast, simple and cheap way to diagnose diseases. Different types of DNA-based nano-biosensors use to support effective deliver personalized medicine [42].

Recently, Quantum dots is based on DNA Nano sensor uses to detect DNA under concentration, fluorescence resonance energy transmission is based on quantum points are reports to behavior as concentrator time's amplification target signals and are points detection using mutations [21].

In addition, Au DE/CYS/RGO/Au NP/ds DNA nano-bio sensors are used together with surface-enhanced Raman spectroscopy (SERS)/electrochemistry transduction to, an anti-psoriatic drug to DNA; the DNA nano-biosensor has the potential to screen drugs by monitoring DNA modification or DNA damage caused by specific antipsoriatic drugs.

Therefore, they have proven to be a useful method for developing anti-psoriatic therapies. In these nano-bio sensors, the embedding of

anti-psoriatic active ingredients in DNA is identified by SERS signals, and electrochemical signals are used to evaluate the effectiveness of active ingredient doses [43].

The double-stranded DNA nano biosensor is composed of a mixture of multi-walled carbon nanotubes (MWNT), colloidal gold nanoparticles (GNP) and GNPMWNT, such as dimethylformamide, 44 sodium dodecyl sulfate and the buffer phosphate or was also used to study the effect of berberine on psoriasis cells through nanometer biosensor, observed berberine DNA triggered by inducing changes in DNA structure U937 breaks in psoriasis cells. Berberine has also been shown to be able to insert from psoriasis The DNA of the cell causes strand breaks, which then opens the DNA helical structure [44].

Extensive research was conducted to understand the possible molecular mechanism of berberine in the biological system to induce its anti-psoriatic effect. For example, an *in vivo* study of in rats with colonic psoriasis deciphered that berberine significantly inhibited cell proliferation. At the cellular level, berberine triggers cell death by inhibiting the mRNA expression of β-catenin in colon psoriasis cells connects with Wnt/β-catenin signaling cascade. According to reports, berberine can also induce autophagy and inhibit cell proliferation in human psoriasis HepG2 and MHCC97 cell lines. Molecule evidence indicates that berberine induces Bax–mediated cell apoptosis by stimulating the activity of caspase 3/9. Molecule berberine interaction is also reported to promote Atg5 apoptosis and autophagy gene. There is sufficient evidence of from the scientific research of that berberine is the up-regulation of Beclin1 gene and promotes the down-regulation of TOR gene. It is worth noting that the MAP Kinase signal cascade and the up-regulation of p53 gene are key molecular processes that promote autophagy in psoriasis cells [45-47].

The side effects of berberine

They are often overlooked due to the low toxicity of berberine. In general, berberine has shown very low toxicity and side effects in animal studies. However, there are definitely some side effects of berberine that need attention. Due to the risk of brain damage caused by bilirubin, jaundice, infants, pregnant women and lactating women should avoid berberine and berberine-containing plants [48]. It has been reported that allergic reactions can occur after intravenous berberine injection [49]. The main side effects are digestion, cramps, diarrhea, flatulence, constipation and stomach pain. Minor side effects include nausea, flatulence, diarrhea, and constipation [50]. High doses of berberine can cause arterial hypotension, dyspnea, flu-like symptoms, heart damage, and gastric disease [49].

Nutrition application formula and diagnosis now through the use of selective nanomaterials, for example, based on antioxidant potential and many other magnetic nanoparticles are used in MRI and FMIR diagnostic procedures with no or limited side effects. Optical and magnetic properties of nanocarriers coupled with active ingredients targeting unit's suitable candidate toxicity significant problem. Hybrid nanostructure Expected nanomedicine will be more in-depth in the future applications of unique element hybrid nano materials, such as cerium with multiple oxidation state and pseudo infinite psoriasis recurrence and transfer [51].

CONCLUSION

Berberine has definite potential as a drug in a wide spectrum of already defined clinical applications. A mounting literature support the concept that berberine and its derivative could be promising drug carrier for psoriasis. It is review that there is various nanotechnology approaches apply to berberine molecule and it is effective against various diseases. The investigation also examined the anti-proliferative effects of berberine and nanotechnology-based repair technology for nano-scale transportation of berberine. Finally, we systematically analyze and examine the current methods and promising viewpoints of the latest hauling of this alkaloid.

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AUTHORS CONTRIBUTIONS

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CONFLICT OF INTERESTS

Declared none

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