ISSN PRINT 2319 1775 Online 2320 7876

Research paper UGC CARE Listed (Group -I) Journal Volume 11,S Iss 3 Dec 2022

Role Of Nanoparticles In The Treatment Of Different Inflammatory Disorders: Boon In The Field Of Medical Science

Mahmood Ahmad Khan[1], Juhi Aggarwal[2], Dr Jyoti Batra[3]

Department of Biochemistry, Santosh Deemed to be University, Ghaziabad, U.P., India

***Correspondence to: Dr JuhiAggarwal,**

Department of Biochemistry, Santosh Deemed to be University, Ghaziabad, U.P.,India

ABSTRACT

The growth of nanoscale molecular probes accomplished of identification, characterization, and medical treatment of disease leads tocreation of imaging technologies. Such probes are significant to inflammationmainly, where the recognition of early disease could simplifytreatment strategy and enhanced, custom-made therapies. This proposes that nanotechnology may offeroutstanding biomarkers for the diagnosis of inflammatory diseases through various techniques like magnetic resonance imaging (MRI), fluorescent quantum dots (QDs), and Raman scattering probes. In this article we will discuss various aspects of NPs in the treatment and diagnosis of inflammation and their applicability in inflammatory diseases.

Keywords: Nanoparticles, inflammation, Biomarkers, magnetic resonance imaging

INTRODUCTION

Historically, Celsus was in the first to define the clinical symptoms of inflammation, who defined four fundamental signs of inflammation such as: “rubor et tumor cum calore et dolore” (redness and swelling with heat and pain). Inflammation signifies a kind of body’s defence mechanism through which the body repairs its tissue and defends itself against various foreign stimulus.These stimulus that causes inflammation can be categorisedon the basis of their origin, may be external or an endogenous agent such as viruses, bacteria, radical oxygen species (ROS), hypoxia etc.(Chovatiya and Medzhitov.,2014). After stimulation a series of event occur involving multiple cell types, such as macrophages, lymphocytes, that secretes cytokines and chemokines, such as tumor necrosis factor (TNF), IL-1,IL-6 etc.. These cytokines produced by theses inflammatory cells not only confiscate other immune cells to the body tissue, they can also proliferate an autoimmune response and inflammation. These cytokines are under the influence of various complex regulatory network such as NF-Kb, MAPK, etc to maintain cytokines level enough to produce inflammation. In inflammation. Disruption of the balance occur between pro- and anti-inflammatory cytokines that has been associated in the pathogenesis of a various inflammatory disorders (McInnesand Schett,2007).Out of all these cytokine it is believed that TNF-α play a vital role in stimulation of other inflammatory cytokines through activation resident macrophages or other cells that led the severity of disease condition like as in rheumatoid arthritis (RA).

ISSN PRINT 2319 1775 Online 2320 7876

Research paper UGC CARE Listed (Group -I) Journal Volume 11,S Iss 3 Dec 2022

Based on its severity and duration, inflammation divided into acute or chronic. Acute inflammation can be defined as short term immune response induced by initial infection or injury (McInnesand Schett,2007), while chronic inflammation occur due to continuous exposure of noxious stimulus for longer duration and Increasing indication suggests that thisplays a pathogenic role in several prevalent diseases including various inflammatory diseases like RA, SLE, psoriasis, cardiovascular, and neurodegenerative (Kamaly et al.,2013), as well as in genetic disease (Paepe and Bleecker,2013). So, to get rid of this lots of work has been carried in the field of medical research and to achieve the very best therapy.Conventionally, main anti-inflammatory drugs are either steroidal such as dexamethasone, prednisone, and (NSAIDS) such as aspirin, ibuprofen, Disease-Modifying Antirheumatic Drugs (DMARDs), and Biologics are used to treat these conditions (Abdulkhaleq et al.,2018). Though both are used to treat inflammatory diseases and give some short of satisfactory results. However, their prolonged use may cause some serious side effects such liver infections, fever, jaundice etc. Therefore, the need of hour to develop a therapeutics that can control inflammation with the aim to obtain greater safety and efficacy,without causing any minimal side effects, and cost effective too(Nordqvist et al.,2017). Targeting TNF-α has been demonstrated as a powerful approach to treat RA using biologics, though, has reduced the progress of arthritis but at the same time it also suppress the immune response against other foreign pathogen that ultimately cause the immune system weak and prone to infections. Recently, Along with the progresses in field of drug development, recently scientists have started working on nano formulationto treat inflammatory diseases i.e. Nanomedicne. This is a new technology that has gained a lot of attention in the last few years known as nanotechnology (Bonifácio et al.,2014).

Nanotechnology has been extensively studied and proved to be apromisingapproach in the healthcare system. This novel technology affords a massive number of nanomaterials and tools that could categorically diagnose and treat different disorders and conditions. This chapter primarily focuses on the current and future potential of nanomedicine to absolutely treat inflammatory disorders. Pharmaceutical industries have become graduallyinvolved in nanomedicine, due to the enormousbenefits this technology provides. Nanomedicinebecome powerful tools for medical research that include targeted drug delivery, materials for tissue engineering, and generatingnanoscaleanalyses for diagnostics and tracking cell movements (Moghimi et al.,2005).

Type of NPs

Different types of NPs are available, and they are fabricated and selectsubjected on different aspects such as the kind of application, Types of nanoparticles

1. Polymeric nanoparticles,
2. Solid lipid nanoparticles (SLNs),
3. Liposomes,
4. Metallic nanoparticles, and

In addition to the above mentioned NPs, there are few more NPs used in the medical research such as Dendrimers, Carbon nanomaterials, Ceramic nanoparticles etc.

ISSN PRINT 2319 1775 Online 2320 7876

Research paper UGC CARE Listed (Group -I) Journal Volume 11,S Iss 3 Dec 2022

Polymer based nanoparticles

Polymeric nanoparticles are most widely used carrier to control drug release and target specific made from biodegradable and biocompatible polymers (Oliveira et al.,2018). Major advantage of Polymeric nanoparticles is that it increase the drug solubility and hence, increasing its absorption and so efficacy, reducing the therapeutic effective dose. They can be nanocapsules or nanospheres and the entity adsorbed to the membrane of nanosphere or nanocapsue. Another way to carry the encapsulated entity is to directly incorporate into matrix or dissolved in the oily core of the polymer(Bonifácio et al.,2014). Two most widely used polymers include polylactic-acid (PLA) and poly-lactic-co-glycolic acid (PLGA) materials that have been used extensively for nanoparticles (Pal et al.,2011).

Solid lipid nanoparticles

Solid lipid nanoparticles (SLNs) are colloidal carrier systems that includes metal based iron, gold and silver NPs. These structures contain purified triglycerides are produced from solid lipids conjugation and are stabilized by surfactants. They are less toxic and more biocompatible, biodegradable than liposome and polymeric NPs(Naahidi et al.,2013). SLNs can be produced on a large scale and offer bettersafeguard against drug degradation (Bonifácio et al.,2014;Naahidi et al.,2013). Their size ranges from 50 to 1000 nm and very much used the field of medical science for the delivery of drugs using different routes such as oral and parenteral routes (Bonifácio et al.,2014).

Lipid based NPs (Liposomes)

Liposomes are classical example of lipid based NPs. It is the most widely used drug delivery system and are small-sized spherical vesicles composed of phospholipid and cholesterol bilayers, separated by an aqueous core (Murthy et al.,2015;Bonifácio et al.,2014). Liposome has high encapsulation capacity and increased circulation time that made it very useful in gather at specific site of disease such as tumor where the endothelial layer is obsolete and liposome collect passively.Polymers like polyethylene glycol (PEG) and the use of saturated lipids, resulted in the creation of stabilized liposomeswith extended half-life and better stability, simultaneously with improving their efficacy (Laverman et al.,2000;Lasic et al.,1991;Sharma et al.,1997). Liposomal drug have also been promising since it confines the side effects of anti-inflammatory drugs on healthy tissues (Bonifácio et al.,2014).

Metallic nanoparticles(Iron oxide, Gold or Silver)

Metallic nanoparticles are made from metals such as titanium, gold, and platinum. They display optical and electronic properties, which make them very worthwhile in the medical field (act as biosensor in living cell)(Yaser et al.,2017). Size of these nanoparticles are ranged from 1 to 100 nm, and they can be modulated with addition of several functional groups, due to their great surface to volume ratio that permits them to be conjugated with various molecules such as antibodies, ligands, and carriers for gene delivery and diagnostic, imaging techniques(Yaser et al.,2017;Harish et al.,2018). Additionally, metallic nanoparticles have the potential to increases the circulatory half-life of drugs that they carry(Naahidi et al.,2013). Metallic NPs are profoundly used in textiles, electronic devices, wound dressings,

ISSN PRINT 2319 1775 Online 2320 7876

Research paper **© 2012 IJFANS. All Rights Reserved, UGC CARE Listed (Group -I) Journal Volume 11,S Iss 3 Dec 2022**

antimicrobial coatings and biomedical devices etc. Examples gold, silver, zinc oxide, and iron nanoparticles.

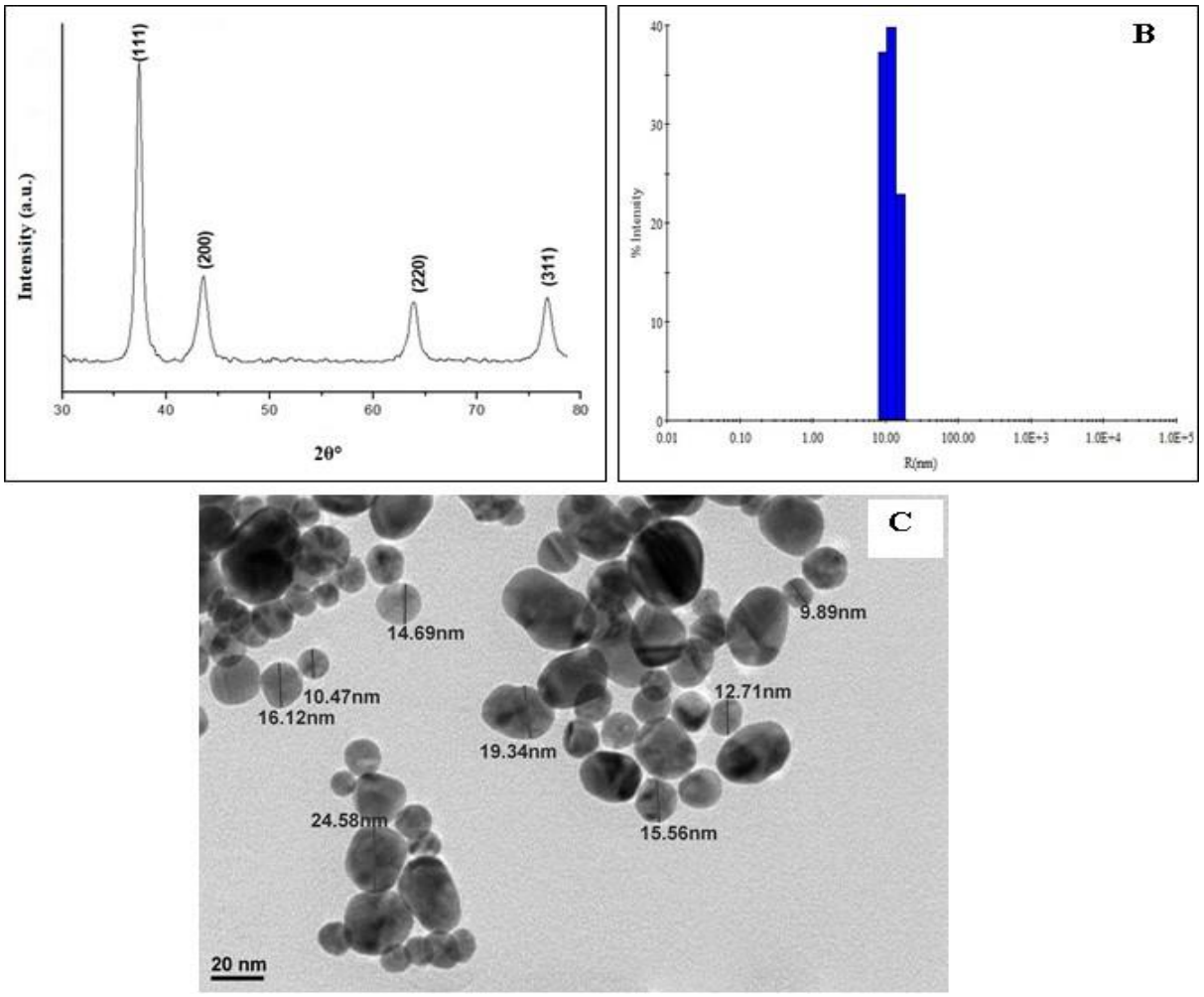

Fig. 1. Characterization of AuNGs. (A) X-ray diffraction pattern of AuNGs (B) DLS measured the hydrodynamic radii of AuNGs. (C) TEM images of AuNGs was recorded with a JEOL JEM-2100F transmission electron microscope (Khan et al.,218)

Significance of Nanomedicine

The major advantagesof nanoparticles (NPs) in the medical research, which created a new field called nanomedicine(Hasan et al.,2018). Due to their Nano size and large surface area, can be used for the diagnosis, prevention, and treatment of many diseases. Due to their lipid soluble property it can easily transported encapsulate drugs, genes, or proteins and protect them from degradation, thus, enhancing their bio distribution and permitting the slow release of drugs with increasing time of exposure to target (Chabib et al.,2018). NPs being tested for molecular imaging in order to accomplish a more specific diagnosis with high-quality images such as magnetic resonance images (MRI), ultrasound, fluorescence, nuclear and computed tomography imaging. They also modulate the bioavailability of water insoluble molecules and so site-specific targeting, hence, diminishing the side effects of drugs.

Contribution of nanoparticles in inflammatory diseases

ISSN PRINT 2319 1775 Online 2320 7876

Research paper UGC CARE Listed (Group -I) Journal Volume 11,S Iss 3 Dec 2022

In modern days, every individual either physicians, or patients have desired for better formulations with increase drug efficacy, low toxicity, and cost effective(Murthy et al.,2015). The orthodox treatments used for inflammatory diseases are normally non-specific treatment options with sever adverse effects. However, use of nanodrug has shown, in many studies over the decade,shows promisingresults, and most of them proved to site specific with reduce side effects and toxicity. Further, it also increase the bioavailability of drug's and effectiveness at the site, and reduce cost. Here we discussed few NPs based treatment in different diseases-

Rheumatoid arthritis and use of NPs in therapeutics

Rheumatoid arthritis (RA) is the most common inflammatory disease (Wagner et al.,2006;Chabib et al.,2018) associated with progressive joint destruction, disability and systemic complications(Oliveira et al.,2018;Chabib et al.,2018). To find a positive result of any treatment is first and most important thing is delivering drugs to the target site directly and this is the major problem nowadays. To solve this problem, bounding drugs to carriers (nanoparticles), makethe delivery most targeting specific and more achievable. Previously, Lee et al.,2013explored the use of nanoparticles in the treatment of RA through near-infrared (NIR) light technology along with the nanoparticles. In this study methotrexate (MTX), was loaded to AuNP which is conjugated with arginine-glycine-aspartic acid (RGD) peptide to the surface of the Au NP forming a multifunctional NP (RGD-MTX-PLGA-Au). In this RGD peptide was used to work as a targeting moiety for inflammation, the Au was used to create heat, and MTX function was to treatment symptoms of RA. After NPs were injected into collagen-induced arthritic (CIA) mice,they were effectively delivered to the target site (inflamed joints) and show better results with lower dose of MTX, when compared to conventional treatment. Further many other authors shows the use of NPs for the treatment of RA (Ilinskayaand Dobrovolskaia,2014)with no or fewer side effects as , in conventional therapy to reach efficacious concentrations in the blood, high doses are given due to their lower bioavailability and rapid clearance from the body, that is associated with severe side effects such as osteoporosis, and hypertension etc. Therefore, using engineered nanomaterials as delivery vehicles is one of the solution to get rid of toxicity and side effects. Recently Khan et al.,2018, successfully reported the use of AuNPs in the treatment of CIA.

Dermatitisand use of NPs

Dermatitis mainly cause inflammation of skin which can be prevented by topical application of some anti-inflammatory drugs such as corticosteroids. Recently, it was reported that, SLN conjugated corticosteroid showed greater result compare to corticosteroids alone (Landriscina et al.,2015). Moreover, SLN cause the sustained release of drug, which is a required for adjusting concentration of drug in skin tissue over time and mayalso improve side effect. In another study, higher local activity of NSAID nanoform when applied to the skin and show better result than NSAID alone(Yokota et al.,2018). Sunscreen is another product applied on skin for the prevention of inflammation caused by ultraviolet (UV) rays. By using UV filters such as titanium oxide (TiO2) and zinc oxide (ZnO), and they are effective in protecting skin against both UVA and UVB rays and using filters in sunscreen formulations for a long

ISSN PRINT 2319 1775 Online 2320 7876

Research paper UGC CARE Listed (Group -I) Journal Volume 11,S Iss 3 Dec 2022

time(Wiechers et al.,2010). Although there has been some apprehension about the use of nanomaterials in sunscreens (Filipe et al.,2009). Hence, additional study is still required to fully estimate the safety of these filters.

Asthma and use of NPs

Asthma is a chronic inflammatory disorder characterized by tightening and swelling of the airways with increased secretion of mucus (Lee et al.,2006). Theophylline is a conventionally used anti allergic drug that had been used since long for the treatment of allergic asthma (Caramori and Adcock,2003). Furthermore, theophylline has severe side effects, which confines its use. The conjugation of theophylline to chitosan (Chitosan is a polymer derived from chitin) nanoparticles, was studied in vivomodels of allergic asthma (Lee et al.,2004) and find theophylline conjugated nanoparticles improved the anti-inflammatory effects of the drug compared to theophylline alone (Lee et al.,2006). Thus, the clinical effects of theophylline in treating asthma could be improved through the use of nanodrug delivery system, which increases bioavailability, adsorption, and residence time of drugs administered through the nasal route(Türker et al.,2004).

Alzheimer's diseaseand use of NPs

AD is a type of chronic neurodegenerative disorder that mostly affects the old age people(Ray and Lahiri,209)that is characterized by cognitive decline and decay in the quality of the patient's life (Darvesh et al.,2012). Anmassive amount of in vivo and in vitro research was performed by groups of researchers to study the outcome of NPs on the management of AD. Albumin NPs loaded tacrine, given through the intranasal route of sheep (Luppi et al.,2011) and found that dendrimers could block the clump of Amyloid β (Aβ), which is the primary reason of AD. This is brought about by the binding to the protofibrils and fibrils, therefore inhibiting the cytotoxic effect of Aβ plaques.

NPsbased Clinical trials

Nanomedicinesshows promising result in treatment of inflammation. For example,Prednisolone-containing liposomes were found to assemble into macrophages of iliofemoral atherosclerosispatients with an increasing circulation half-life, in contrast to the experimental data recorded in rabbits (Lobatto et al.,2010). Though short-term treatment did not show any significant result on arterial wall permeability or inflammation (van der Valk et al.,215). Probably due to insufficient dose and time of prednisolone reaching the plaque. In another study author reported that targeted delivery of nanomedicines to atherosclerotic lesions is possible in humans, could offerdirection for the development of future nano-formulations for treatment of atherosclerosis.

Recently, pilot clinical study shows trans- retinoic acid (Tretinoin), have good efficacy against acne(Sabouriet al.,2018). Similarly, silica gold nanoshell coated with PEG treatment against focal thermolysis of sebaceous gland,provide a noteworthydecrease in occurrence and appearance of inflammatory lesions (https://www.prnewswire.com/news-releases,2019).Finally we can say that, very limitednanomedicines designed for the management of inflammation and assessed through clinical trials. In order to workin transformation from the bench to the bedside, numerous challenges need to be addressed.

ISSN PRINT 2319 1775 Online 2320 7876

Research paper UGC CARE Listed (Group -I) Journal Volume 11,S Iss 3 Dec 2022

Upcomingvisions

Anti-inflammatory effects of engineered nanomaterials can be deliberatelyreached by modifying the physicochemical properties of nanoparticle and by using nanoparticles as carriers fordrugs. Further, structure activity relationship (SAR) studies are also required furtherto improve nanotechnology. In addition, to the reported advantages that nanoparticle holds as drug carriers, large number of disadvantages are also reported (Chabib et al.,2018). For example, NPs might generate toxicity due to their small size, which widen the biodistribution of the drug in the body. Hence, used of NPs is two headed sword thatin one hand increases the drugs' potency, and in other hand at it also might affect the immune system of the body and trigger toxicity (Bonifácio et al.,2018). Therefore, future nanodrug studies should also focus on toxicity and on recognizingthe key elements like composition, dose, route of administration, physicochemical properties that might incite toxicity. This will aid drug delivery formulation through selecting right nanoparticle carriers and will clearly improve the rapidly growing field of nanodrug delivery.

CONCLUSION

Most drugs currently used now a days are inadequate by their non-specific in nature, poor solubility, high cost, and number of side effects. Therefore, scientists are in continuous search for discovery of new drugs. Using NPsfor the delivery of drugs is one step to avoid those limitations. NPs are now studied to simultaneous delivery of two or more drugs for blend therapy, targeting to lower the rateor frequency of medications a patient is receiving, decreasing chance of toxicity and also reduces the economic burden on patients. The keybenefit of using NPs is that dose and target specificity could be modulated very easily to match the need. Therefore, development of NPs as carriersof drug delivery can offer new opportunities to achieve precise treatment of diseases and improve the possible therapeutic effectiveness of conventional medications, thatimprove the socio economic burden and quality of life.

REFERENCES

ChovatiyaR., MedzhitovR.Stress, inflammation, and defense of homeostasis, Mol. Cell 54 (2014) 281–288.

McInnes, I.B. and Schett, G. Nat. Rev. Immunol.(2007) 7, 429–442.

N. Kamaly, G. Fredman, M. Subramanian, S. Gadde, A. Pesic, L. Cheung, Z. A. Fayad, R. Langer, I. Tabas, O. C. Farokhzad, Development and in vivo efficacy of targeted polymeric inflammation-resolving nanoparticles. Proc. Natl. Acad. Sci. U.S.A. 110, 6506–6511 (2013)

B. D. Paepe, J. L. De Bleecker, Cytokines and chemokinesasregulatorsofskeletal muscle inflammation: Presenting the case of Duchenne muscular dystrophy. Mediators Inflamm. 2013, 540370–540380 (2013).

Abdulkhaleq LA, Assi MA, Abdullah R, Zamri-Saad M, TaufiqYap YH, Hezmee MNM. The crucial roles of inflammatory mediators in inflammation: A review. Veterinary World. 2018;11(5):627-635

ISSN PRINT 2319 1775 Online 2320 7876

Research paper UGC CARE Listed (Group -I) Journal Volume 11,S Iss 3 Dec 2022

Nordqvist C. Everything You Need to Know About Inflammation. Medical News TodayMedilexicon. 2017.

Bonifácio BV, da Silva PB, dos S Ramos MA, Negri KMS, Bauab TM, Chorilli M. Nanotechnology-based drug delivery systems and herbal medicines: A review. International Journal of Nanomedicine. 2014;9:1-15

Moghimi SM, Hunter AC, Murray JC. Nanomedicine: Current status and future prospects. The FASEB Journal. 2005;19(3):311-330.

Oliveira IM, Gonçalves C, Reis RL, Oliveira JM. Engineering nanoparticles for targeting rheumatoid arthritis: Past, present, and future trends. Nano Research. 2018;11(9):4489-4506

Pal SL, Jana U, Manna PK, Mohanta GP, Manavalan R. Nanoparticle: An overview of preparation and characterization. Journal of Applied Pharmaceutical Science. 2011;1(6):228-234

Naahidi S, Jafari M, Edalat F, Raymond K, Khademhosseini A, Chen P. Biocompatibility of engineered nanoparticles for drug delivery. Journal of Controlled Release. 2013;166(2):182-194

Murthy S, Papazoglou E, Kanagarajan NMNS. Nanotechnology: Towards the detection and treatment of inflammatory diseases. In: Stevenson CS, Marshall LA, Morgan DW, editors. In Vivo Models of Inflammation. Progress in Inflammation Research. Switzerland: Birkhäuser Basel; 2006.

Laverman, P., Brouwers, A.H., Dams, E.T., Oyen, W.J., Storm, G., van Rooijen, N., Corstens, F.H.,Boerman, O.C. Preclinical and clinical evidence for disappearance of long-circulating characteristics of polyethylene glycol liposomes at low lipid dose. J. Pharmacol. Exp. Ther. 2000, 293, 996–1001. 37.

Lasic, D.D., Martin, F.J., Gabizon, A., Huang, S.K.,Papahadjopoulos, D. Sterically stabilized liposomes: A hypothesis on the molecular origin of the extended circulation times. Biochim. Biophys. Acta 1991, 1070, 187–192.

Sharma, U.S., Sharma, A., Chau, R.I.,Straubinger, R.M. Liposome-mediated therapy of intracranial brain tumors in a rat model. Pharm. Res. 1997, 14, 992–998.

Yaser D, Hoda J, Jiafu C, Al-Chick Sulaiman B. Nanoparticles. In: Yaser D, editor. Nanotechnology and Functional Materials for Engineers. Philadelphia, United States: Elsevier; 2017. pp. 93-119

Harish KK, Nagasamy V, Himangshu B, Anuttam K. Metallic nanoparticle: A review. Biomedical Journal of Scientific & Technical Research 2018;4(2):1-11.

Hasan A, Morshed M, Memic A, Hassan S, Webster TJ, Marei HES. Nanoparticles in tissue engineering: Applications, challenges and prospects. International Journal of Nanomedicine. 2018;13:5637-5655

Chabib L, Ikawati Z, Martien R, Ismail H, Wahyudi MDP, Arimurni DA, et al. Rheumatoid arthritis and the challenge of using nanoparticles for its treatment. MATEC Web of Conferences. 2018;154:1-7

Wagner V, Dullaart A, Bock A-K, Zweck A. The emerging nanomedicine landscape. Nature Biotechnology. 2006;24:1211-1217

ISSN PRINT 2319 1775 Online 2320 7876

Research paper **© 2012 IJFANS. All Rights Reserved, UGC CARE Listed (Group -I) Journal Volume 11,S Iss 3 Dec 2022**

Lee S-M, Kim HJ, Ha Y-J, Park YN, Lee S-K, Park Y-B, et al. Targeted chemo-photothermal treatments of rheumatoid arthritis using gold halfshell multifunctional nanoparticles. ACS Nano [Internet]. 2013;7(1):50-57.

Ilinskaya AN, DobrovolskaiaMA. Immunosuppressive and anti-inflammatory properties of engineered nanomaterials. British Journal of Pharmacology. 2014;171(17):3988-4000.

Landriscina A, Rosen J, Friedman A. Nanotechnology, inflammation and the skin barrier: Innovative approaches for skin health and cosmesis. Cosmetics. 2015;2(2):177- 186.

Yokota J, Kyotani S. Influence of nanoparticle size on the skin penetration, skin retention and anti-inflammatory activity of non-steroidal anti-inflammatory drugs. Journal of the Chinese Medical Association - Elsevier Ltd. 2018;81(6):511-519

Wiechers JW, Musee N. Engineered inorganic nanoparticles and cosmetics: Facts, issues, knowledge gaps and challenges. Journal of Biomedical Nanotechnology. Oct 2010;6(5):408-431

Filipe P, Silva JN, Silva R, Cirne De Castro JL, Marques Gomes M, Alves LC, et al. Stratum corneum is an effective barrier to TiO2 and ZnO nanoparticle percutaneous absorption. Skin Pharmacology and Physiology. 2009;22(5):266-275

Lee DW, Shirley SA, Lockey RF, Mohapatra SS. Thiolated chitosan nanoparticles enhance antiinflammatory effects of intranasally delivered theophylline. Respiratory Research. 2006;7(1):-10

Caramori G, Adcock I. Pharmacology of airway inflammation in asthma and COPD. Pulmonary Pharmacology & Therapeutics. 2003;16(5):247-277

Lee DW, Powers K, Baney R. Physicochemical properties and blood compatibility of acylated chitosan nanoparticles. Carbohydrate Polymers. 2004;58:371-377

Türker S, Onur E, Özer Y. Nasal route and drug delivery systems. Pharmacy World & Science. 2004;26(3):137-142

Ray B, Lahiri DK. Neuroinflammation in Alzheimer's disease: Different molecular targets and potential therapeutic agents including curcumin. Current Opinion in Pharmacology. 2009;9(4):434-444

Darvesh AS, Carroll RT, Bishayee A, Novotny NA, Geldenhuys WJ, Van der Schyf CJ. Curcumin and neurodegenerative diseases: A perspective. Expert Opinion on Investigational Drugs. 2012;21(8):1123-1140

Luppi B, Bigucci F, Corace G, Delucca A, Cerchiara T, Sorrenti M, et al. Albumin nanoparticles carrying cyclodextrins for nasal delivery of the anti-Alzheimer drug tacrine. European Journal of Pharmaceutical Sciences. 20 Nov 2011;44(4):559-565

M.E. Lobatto, Z.A. Fayad, S. Silvera, E. Vucic, C. Calcagno, V. Mani, S.D. Dickson, K. Nicolay, M. Banciu, R.M. Schiffelers, J.M. Metselaar, L. van Bloois, H.S. Wu, J.T. Fallon, J.H. Rudd, V. Fuster, E.A. Fisher, G. Storm, W.J. Mulder, Multimodal clinical imaging to longitudinally assess a nanomedical anti-inflammatory treatment in experimental atherosclerosis, Mol. Pharm. 7 (2010) 2020–2029.

F.M. van der Valk, D.F. van Wijk, M.E. Lobatto, H.J. Verberne, G. Storm, M.C. Willems, D.A. Legemate, A.J. Nederveen, C. Calcagno, V. Mani, S. Ramachandran, M.P. Paridaans,

ISSN PRINT 2319 1775 Online 2320 7876

Research paper UGC CARE Listed (Group -I) Journal Volume 11,S Iss 3 Dec 2022

M.J. Otten, G.M. Dallinga-Thie, Z.A. Fayad, M. Nieuwdorp, D.M. Schulte, J.M. Metselaar, W.J. Mulder, E.S. Stroes, Prednisolone-containing liposomes accumulate in human atherosclerotic macrophages upon intravenous administration, Nanomedicine 11 (2015) 1039–1046.

M. Sabouri, A. Samadi, S. Ahmad Nasrollahi, E.S. Farboud, B. Mirrahimi, H. Hassanzadeh, M. NassiriKashani, R. Dinarvand, A. Firooz, Tretinoin loaded nanoemulsion for acne vulgaris: fabrication, physicochemical and clinical efficacy assessments, Skin Pharmacol. Physiol. 31 (2018) 316–323.

S.A.P.R.o.T.I.C.S.i.A. S. Inc, (n.d.) https://www.prnewswire.com/news-releases/ sebacia-announces-positive-results-of-two-independent-clinical-studies-in-acne300026759.html 2019