ejpmr, 2024, 11(6), 409-420.

SJIF Impact Factor 7.065

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Review Article

ISSN 2394-3211

EJPMR

NANOTECHNOLOGY: A POTENTIAL APPROACH FOR DIABETIC PATIENTS

Aditi Daiwalkar*, Dr. Nitin Padole, Dr. Nilakshi Dhoble, Dr. Pankaj Dhapke and Dr. Jagdish Baheti

Department of Pharmaceutics, Kamla Nehru College of Pharmacy, Butibori Nagpur Maharashtra (India)-441108.

***Corresponding Author: Aditi Daiwalkar**

Department of Pharmaceutics, Kamla Nehru College of Pharmacy, Butibori Nagpur Maharashtra (India)-441108.

Article Received on 19/04/2024 **Article Revised on 09/05/2024** **Article Accepted on 29/05/2024**

ABSTRACT

Diabetes Mellitus is a unique metabolic disease characterized by a change in blood sugar balance. Recently, there has been an increased focus on using nanotechnology to create novel medicine delivery systems. When compared to other traditional medication delivery method, the nanoparticles have a number of advantages. Owing of their altered physical, chemical, biological properties, nanoparticles have played a significant role in technological breakthroughs. Because of their tiny size, nanoparticles can easily migrate throughout the body and enter highly complex organ an array of pathway. Nanoparticle are best possible drug delivery technology due of their excellent stability and regulate drug release, they provide flexibility in the administration approach. Drugs that are hydrophilic as well as hydrophobic can be administered as nanoparticles. Basically, nanotechnology offers a wide range of strategies to reduce effective dose of medications while maintaining or even improving their therapeutic efficacy. These approaches can benefit patients by reducing adverse effects and enhancing the overall safety and effectiveness of drug therapies in various medical conditions, including cancer, diabetes and many other diseases. This review mostly concentrates on methodology that is used for nanotechnology that is types and method of preparation of nanoparticles for diabetic mellitus.

KEYWORDS: Diabetes Mellitus, Nanotechnology, Nanoparticles, Milling, Co-Precipitation.

INTRODUCTION

Diabetes Mellites

Diabetes has among the biggest worldwide health and economical burden to all over the world. The primary diabetes marker is hyperglycaemia. Diabetes is a dangerous long-term ailment that has a significant influence on people's lives, families & societies around the world. According to estimates, it was one of the top 10 causes of adult deaths and contributed to four million fatalities worldwide in 2017.[1]

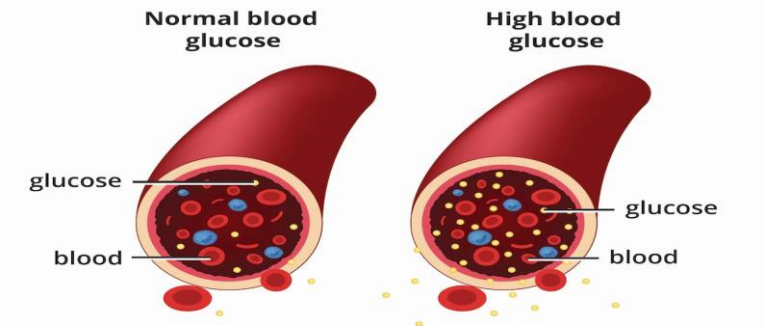


Figure 1: Comparison of normal blood glucose & high blood glucose of diabetic patient.

Some people lose β-cell quickly, while others lose them slowly. Although it is frequently seen in youngsters, the quickly progressing variant of T1DM can also affect adult. Ketoacidosis the initial indication of the illness in certain people, especially children and adolescents. Other may have mild hyperglycaemia that, in the event of an illness or another stressful situation, might quickly worsen into hyperglycaemia and/or ketoacidosis. Obesity is seen for those with T1DM and is on the rise in the general population. Insulin independent diabetes is another name for type 2 diabetes. There are several different medications available to treat and control blood sugar. The term known as type 2 diabetes is brought on by issues with how body control and uses sugar as fuel.[2]

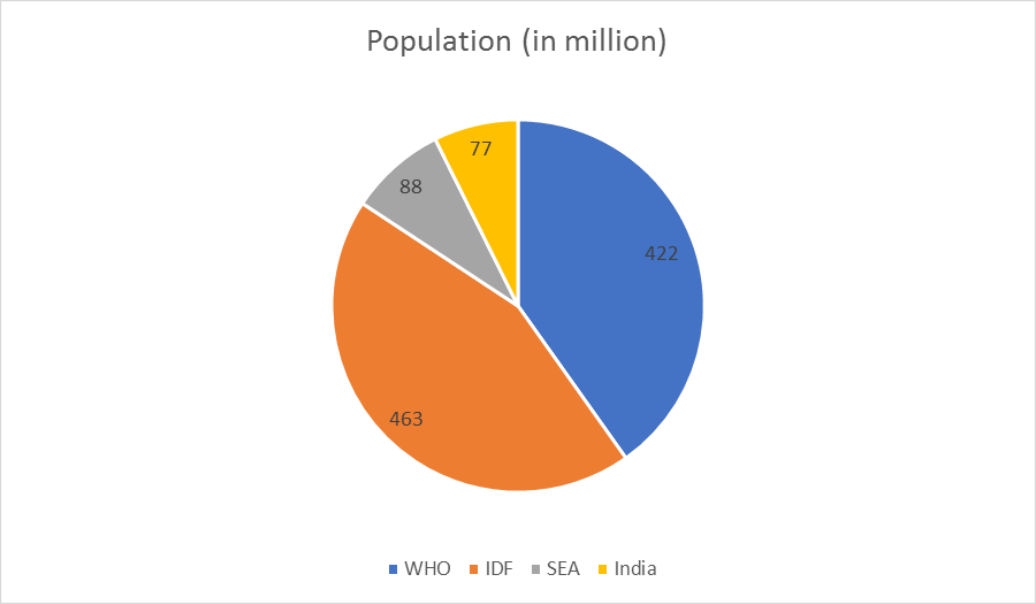


Figure 2: Population of Diabetic Patient in the world.

Pathophysiology of type 2 diabetes (NIDDM)

The cause of diabetes depends on the type of diabetes. Type 1 occurs mainly due to β-cell destruction, mediated through either immune mediated or idiopathic, whereas Type 2 diabetes occurs mainly due to insulin resistance or with relative insulin deficiency.[3]

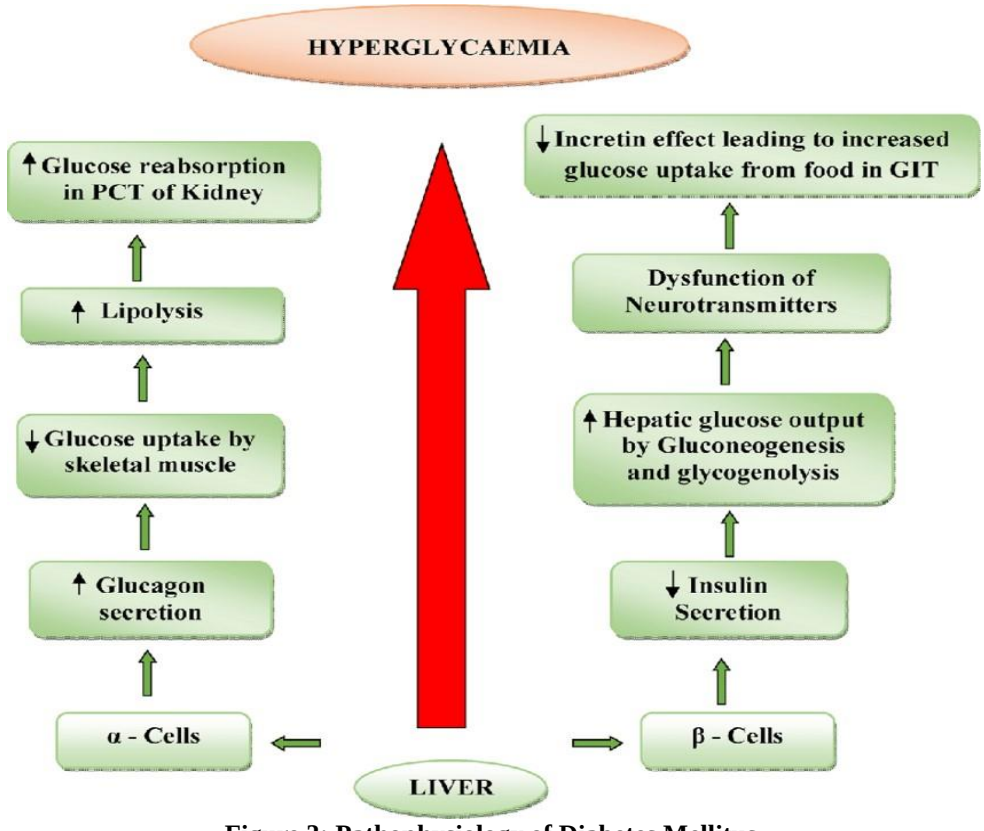


Figure 3: Pathophysiology of Diabetes Mellitus.

Mechanism of Diabetes[3]

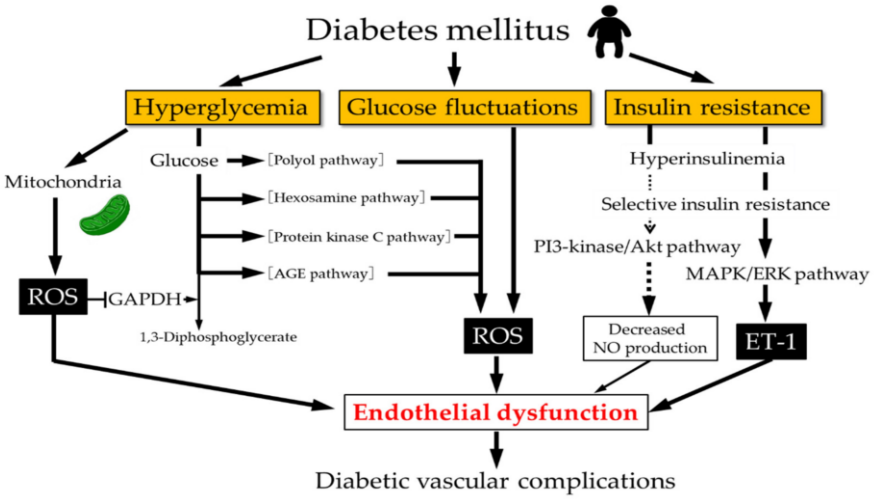


Figure 4: Mechanism of diabetes.

Treatment of Diabetes Mellitus[4,5]

Table 1: Treatment of Diabetes Mellitus.

Name of Drug	Categories	Mechanism of Action
Canagliflozin	Sodium glucose co-transporter 2 (SGLT2)	inhibiting SGLT2 in PCT, to prevent reabsorption of glucose and facilitate its excretion in urine.
Sitagliptin, Saxagliptin, linagliptin	DPP-4 inhibitor	blocking the action of DPP-4, an enzyme which destroys the hormone incretin.
Tirzepatide,	GLP1 & DUAL GLP-1\GIP receptor agonist	insulin secretion and attenuate postprandial excursions of glucose.
Acarbose, Miglitol	α glucosidase inhibitor	inhibit the absorption of carbohydrates from the small intestine.

Diagnostic Tests for Diabetes Mellitus

Table 2: Diagnostic test of Diabetes Mellitus.

	Normal	Prediabetic	Diabetic
A1C	≤5.6 %	5.7-6.4 %	≥6.5 %
FPG	≤99 mg/dL	100-125 mg/dL (5.6- 6.9 mmol/L)	≥ 126 mg/dL (7.0 mmol/L)
OGTT	1313≤139 mg/dL	100-140-199 mg/dL (7.8-11.0 mmol/L)	≥ 200 mg/dL (11.1 mmol/
RPG	RPG		≥ 200 mg/dL (11.1 mmol/L)

Nanotechnology

The phrase "Nanotechnology" refers to the process of manipulating matter at the atomic, molecular and supramolecular level, where special quantum mechanical effects occur. In the 21st century, nanotechnology is a novel and crucial technology. Single atoms and molecules are used in this type of science and technology to create materials. It examines the uses and characteristics of material with structures ranging from 0.1 to 100nm in size.[6]

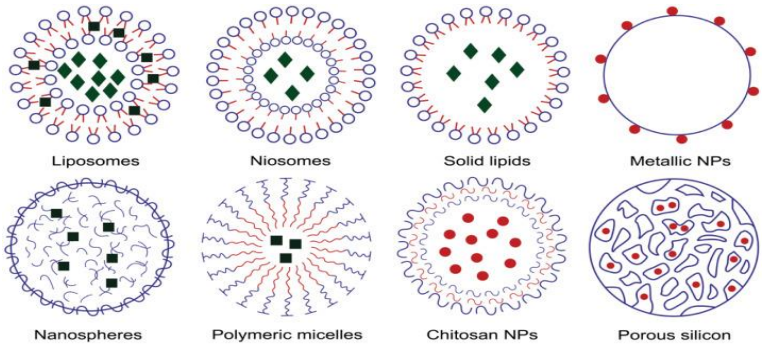


Figure 5: Different types of nanocarrier that prevent diabetes.

Nanoparticles

There are several nanoparticles-based delivery systems that have been suggested to improve penetration across the gastrointestinal tract and avoid enzymatic breakdown in the stomach in order to improve oral insulin absorption. Due to benefits including the capacity to incorporate hydrophobic/hydrophilic drugs, drug targeting, avoiding organic solvents, good tolerance and stability and scaling up practicality, solid lipid nanoparticles have drawn more attention innovative nanoparticles drug carriers. Solid lipid nanoparticles taken orally show lymphatic drug transport as their main mode of drug absorption and bypass first pass digestion.[7,8]

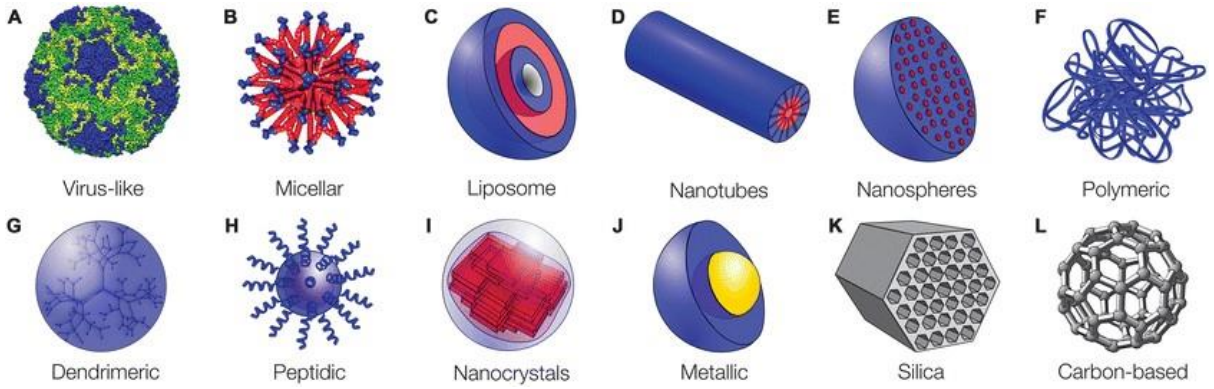
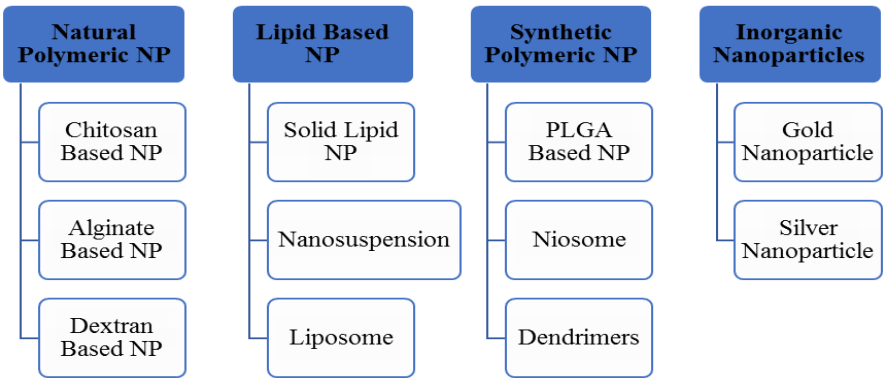


Figure 6: Structure of Different Types of Nanoparticles.

Advantages of Nanoparticles

- Drug delivery system using nanoparticles are more stable.
- Nanoparticles have a greater carrying capacity.
- Nanoparticles are biodegradable, non-toxic and can be kept for longer periods of time.
- Nanoparticles can also be used for controlled delivery of drug.[9]

Types of Nanoparticles



1. Natural Polymeric Nanoparticles

a) Chitosan Based Nanoparticles: The degree of deacetylation from chitin and molecular weight, as well as the pH level, are in charge of Chitosan's physiochemical characteristics, which include a positive surface charge that forms hydrogen and the mucin's sialic acid group is connected via electrostatic ionic connections.[10,11]

b) Alginate-Based Nanoparticles: An anionic polysaccharide called alginate is made up of blocks of (1-4)-linked d-mannuronic acid and l-guluronic acid residues that alternate. It is a mucoadhesive, pH-sensitive, hydrophilic, biodegradable, and biocompatible polymer. Due to the polymer's guluronic acid residues, which can bind with divalent ions to form a gel matrix by exchanging sodium ions, insulin can be retained in the nanoparticles. When the peptide was loaded into alginate-chitosan nanoparticles created by ionotropic pre-gelation, the insulin helix and sheet were preserved.[12]

c) Dextran-Based Nanoparticles: Dextran is a negatively charged, hydrophilic, biodegradable, and biocompatible polysaccharide that can bind to proteins and positively charged chitosan. The nano emulsion dispersion method and in situ gelation have been suggested as a way to load insulin into alginate-dextran nanoparticles. Alginate limits insulin release by forming a tight matrix at pH 1.2, but at pH 7.4, the matrix opens up and releases the peptide.[13,14]

2. Synthetic Polymeric Nanoparticles

a) PLGA Based Nanoparticles: Synthetic polymer PLGA is one of the most widely used materials for creating drug-delivery nanoparticles because of its biodegradability and biocompatibility. Due to their

typical negative charge, PLGA nanoparticles have trouble penetrating the negatively charged mucus layer. It has been suggested that cationic chitosan be used as a coating to change the surface charge of the particles in order to increase the GIT mucoadhesive Ness of PLGA nanoparticles. To improve the GI uptake of insulin through M cells and folate receptors, another nanoparticle formulation that conjugated folate and PEGylated PLGA was employed.[15]

b) Other Polymeric Nanoparticles Containing CPP: Bis-β-CD changed penetrating, a cell penetrating peptide (CPP), to create a nanocomplex. It made it easier for negatively charged insulin to pass through the epithelial layer by energy-dependent endocytosis and energy-independent transduction. Studies on the absorption of both modified and unmodified nanocomplexes in vitro and in situ have demonstrated that the modified nanocomplex caused more insulin to permeate than the unmodified nanocomplex.[16,17]

c) Poly (Lactic Acid) (PLA)-Based Nanoparticles: For oral medication delivery, PLA, a biodegradable and biocompatible polymer, is typically utilized. A vesicle made of polymeric PLA-b-Pluronic-b-PLA (PLAF127-PLA) was used to deliver insulin orally. While these nanoparticles did elicit hypoglycaemic effects, they exhibited an initial burst release of insulin, resulting in localized gastrointestinal toxicity.[18]

d) Niosomes: Niosomes are artificial nanometric vesicles that are stabilized by cholesterol and rearranged into concentric bilayers using non-ionic surfactants such as amides, esters, and alkyl ethers. They are categorized as small unilamellar vesicles (SUV; 10–100 nm), large unilamellar vesicles (LUV; 100–3000 nm), or multilamellar vesicles (MLV), which are similar to liposomes, based on their sizes and bilayers. When a high drug payload is present, niosomes can function as drug reservoirs to produce sustained or extended release. Because of the hydrophilic, amphiphilic, and lipophilic moieties that make up their structure, they have the ability to accommodate drugs with varying solubility.[19,21]

3. Inorganic Nanoparticles: The delivery of insulin orally has also been investigated using inorganic nanoparticles. Insulin-loaded gold nanoparticles were found to be non-toxic and biocompatible in diabetic rats, effectively lowering blood sugar levels through both oral and intranasal delivery.[22,23]

a) Gold Nanoparticles: GNPs range in size from 2 to 100 nm, although the most effective cellular uptake was seen in the 20–50 nm particle size range. Particles with a diameter of 40–50 nm have demonstrated specific cell toxicity. The following are some of the benefits of GNPs: they are biocompatible, have distinct physical and chemical characteristics that improve drug loading, are non-cytotoxic to healthy cells, and can be manufactured in a variety of ways.[24,25]

b) Silver Nanoparticles: Before the recent dawn of the nanotechnology period, when it was realized that silver could be created at the nanoscale, it was only known as a metal. Modern engineering techniques have been applied to metallic silver, producing ultrafine particles with sizes measured in nanometres (nm) and unique shapes and properties.[26,27]

4. Lipid-Based Nanocarriers

a) Solid Lipid Nanoparticles: Solid lipid nanoparticles, or SLNs, are submicron-sized particles (50–1000 nm) made up of an aqueous dispersion of a surfactant encircling a crystalline lipid core. SLNs have been shown to improve drug absorption when taken orally because they follow the same metabolic pathways as dietary lipids. The physiological properties of SLNs, which are made of lipids that closely resemble those in the human body and have high biocompatibility and biodegradability, make them advantageous for use as drug delivery systems. Various solid lipid nanoparticle (SLN) formulations have been developed for insulin loading.[28]

b) Nanostructured Lipid Carriers (NLCs): SLN is not the same as nanostructured lipid carriers (NLCs), which are composed of a mixture of liquid and solid lipids that stay solid at room temperature and body temperature. Higher loading capacities for lipophilic compounds and better drug release modelling are two benefits that NLCs have over SLNs. Lately, there has been talk of using essential oils with hypoglycaemic qualities as the active component of NLCs of the DM management.[29,30]

c) Liposomes: Liposomes are tiny vesicles made of cholesterol and one or more phospholipid bilayers that are naturally occurring and non-toxic. They are employed in drug delivery due to their low toxicity, biodegradability, ability to entrap hydrophilic and lipophilic drugs, and usefulness for site-specific/targeted delivery. Numerous strategies have been put forth that use liposomes to target particular cells to improve efficacy and safety and to lessen the toxicity of loaded drugs.[31,32]

d) Nano emulsion: Colloidal scattering frameworks known as Nano emulsions possess thermodynamic stability and are composed of two immiscible liquids combined with co-surfactants and surfactants, which act as emulsifying agents, to create a single phase. An emulsifier, water, and oil make up a Nano emulsion.[33,34]

e) Drug Nanosuspension: Another delivery system that can be used for oral administration is drug nanosuspensions, also known as drug nanocrystals. In these systems, the active ingredients are in the solid state and have a particle size of up to 1 µm, surrounded by a

hydrophilic surfactant in an aqueous dispersion. To increase the solubility of medications classified as BCS II and IV by the Biopharmaceutical Classification System (BCS), drug nanosuspensions have been proposed.[35,36]

Method of Preparation of Nanoparticles[37]

1. Physical Method
2. Chemical Method
3. Biological Method.

A. Physical Method

a) Ball Milling

Clever techniques for producing nanoparticles. Planetary, vibratory, rod, and tumbler mills are some of the types in use. Hard balls composed of steel or carbide are inside the container. Nanocrystalline Silicone using this technique, Cr, W, and Ag-Fe are synthesized. Balls to the ratio of 2:1 for materials.[38,40]

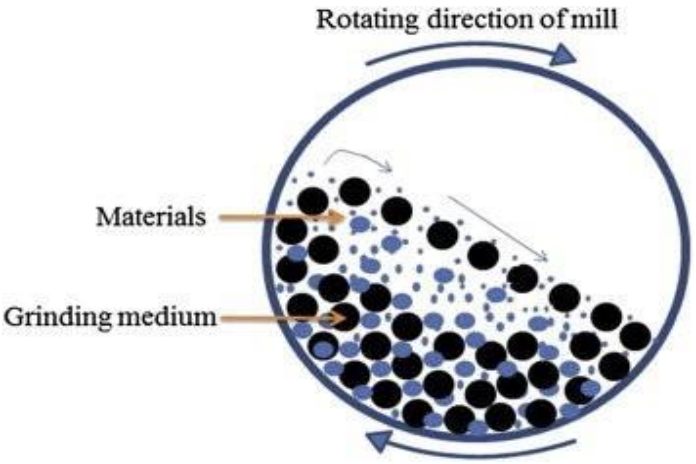


Figure 7: Ball Mill.

b) Melt Mixing: Nanoparticles are created when molten metal streams are mixed with turbulence at a high speed. In a glass, nanoparticles are arrested. Glass is an amorphous solid with an imperfectly symmetrical atom or molecular structure. Metals can form amorphous solids, or metallic glasses, when cooled to extremely high cooling temperatures.[41,42]

c) Pulse Laser Ablation: A vacuum chamber is filled with the target sample. When the sample is exposed to a high-pulsed laser beam, plasma is created and subsequently converted into a colloidal solution of nanoparticles. When creating nanoparticles, the second-harmonic group type laser is widely employed. The type of laser, a few pulses, the type of solvent, and the pulsing time are factors that influence the final product.[43]

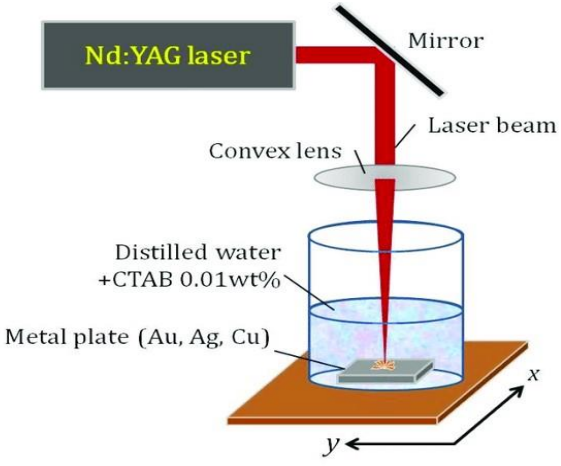


Figure 8: Pulse Laser Ablation.

d) Chemical Vapour Deposition: At between 300 and 1200 °C, a thin layer of gaseous reactant is deposited on the substrate. A thin layer of product forms on the substrate's surface as a result of a chemical reaction between a heated substrate and combining gas. The applied pressure fluctuates between 100 and 105 Pa. The method produces rigid, homogeneous, durable, and extremely pure nanoparticles, which are its benefits. In order to remove the by-products from the substrate, they must be transported back to the gaseous phase.[45]

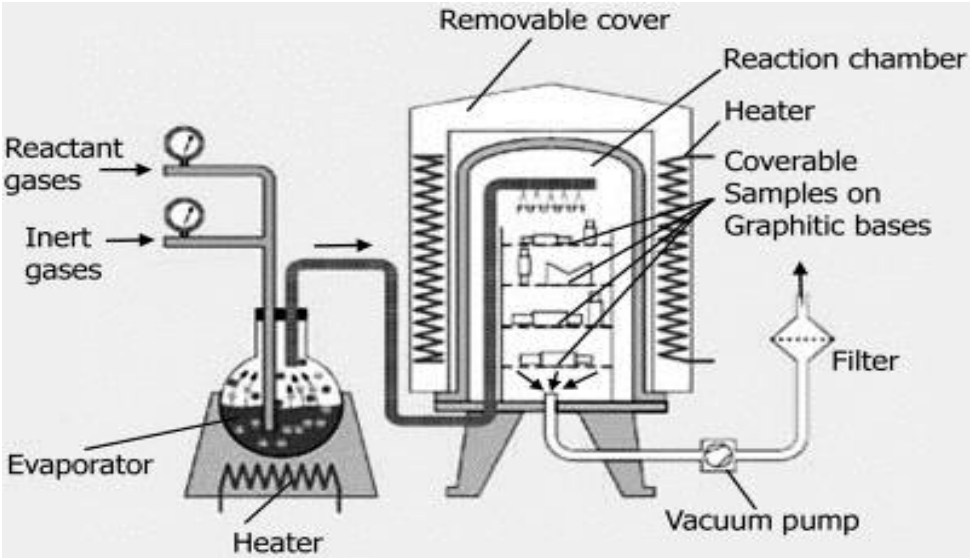


Figure 9: Chemical Vapour Deposition.

B. Chemical Method

i) Sol Gel Method

It includes the condensation, hydrolysis, and thermal breakdown of metal precursors or alkoxides in a solution. The result is the formation of a stable solution, or sol. Increased viscosity is created in the gel upon hydrolysis or condensation. By adjusting the pH, temperature, and precursor concentration, the particle size can be observed. It may take a few days for the solvent to be removed, Ostwald ripening to occur, and phase change to occur. A mature step is necessary to support the growth of solid mass. In order to create nanoparticles, the unstable reagents are separated.[46]

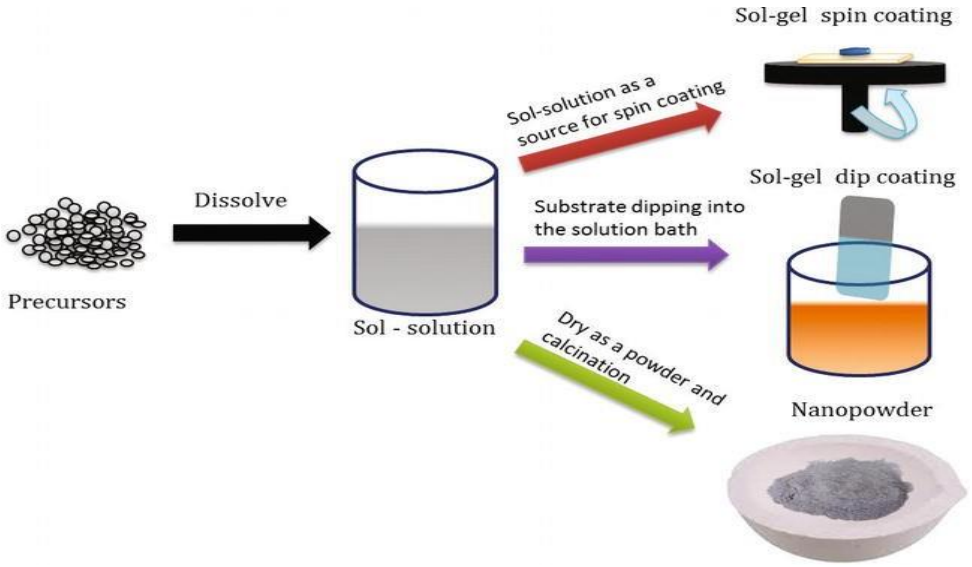


Figure 10: Sol Gel Method.

ii) Sonochemical Synthesis

Pd-CuO nanohybrids have been successfully created by sonochemically fusing copper salt with palladium in the presence of water. With the use of ultrasonic waves, switch metal salts might be changed into their oxides in the presence of palladium and water. The palladium supply is either the palladium salts or pure metallic palladium.[47]

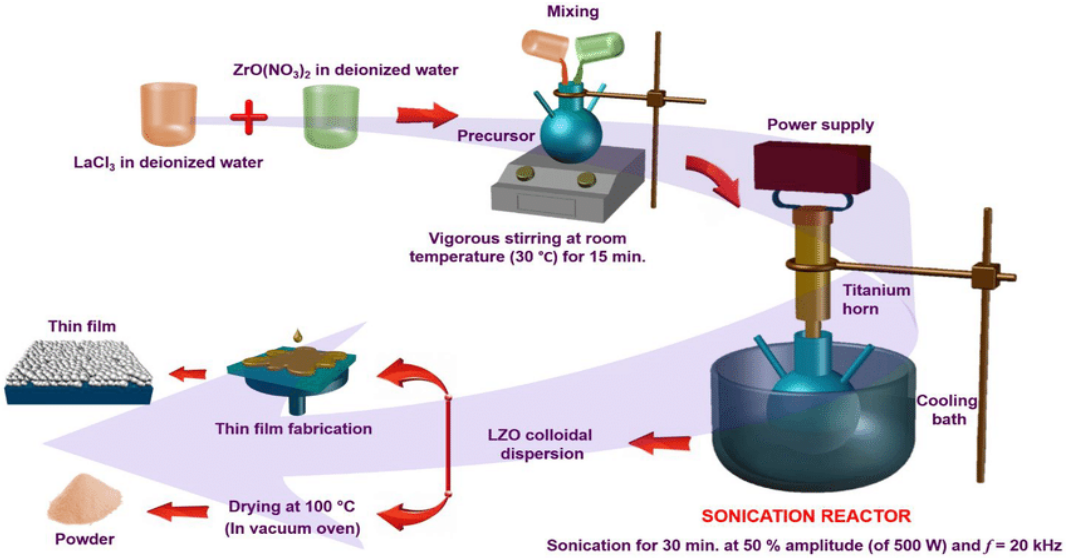


Figure 11: Sonochemical Synthesis.

iii) Co-Precipitation Method

Another name for this wet chemical process is solvent displacement method. Ethanol, acetone, hexane, and nonsolvent polymers are example of polymer solvent. Polymer phase might be synthetic or natural. When the polymer solution is finally mixed, the rapid diffusion of the polymer solvent into the nonsolvent polymer phase result in the production of nanoparticles due to interfacial tension between two phases.[48]

Figure 12: Co-precipitation method.

C. Biological Method

1. Synthesis Using Plant Extract

Plant extract has a crucial role in nanoparticles production. This method is also known as "Green Synthesis or Green process manufacturing". To make gold nanoparticles, geranium (pelargonium graveolens) plant leaves have been employed. To create silver nanoparticles, 1 ml of mmol aqueous solution of silver nitrate is mixed with 5 ml of plant extract. The procedure for synthesizing from alcoholic extract is the same. Silver nitrate and plant extract are stored in a shaker with 150rpm in the dark.[49]

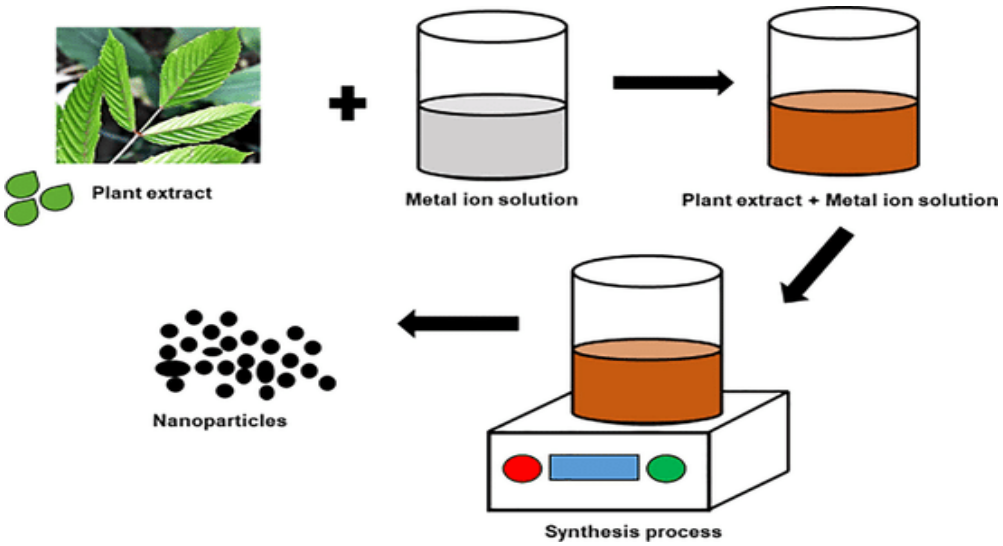


Figure 13: Green Synthesis Method.

Evaluation Parameter for Nanoparticles

1. Particle Size and Zeta Potential: Using a Horiba scientific nanoparticle instrument, the dynamic light scattering technique was used to measure the particle size. Electrophoretic mobility in the presence of an electric field was used to estimate zeta potential.[50]

2. Drug Entrapment Efficiency: Measuring the concentration of free drugs in the dispersion medium allowed researchers to calculate the drug's entrapment efficiency. A 10 mg freeze-dried drug was dissolved in aliquot volumes of pH 7.4 phosphate buffer, and the mixture was filtered through membrane filters with a pore size of 0.45 µm. Absorbance of the filtered solutions were recorded by UV-visible spectrophotometer Using the following formula, the percentage entrapment efficiency (% EE) was determined.[51]

% EE = (drug mass in submicron particles) / (drug mass in formulation) × 100.

3. Shape & Surface Morphology: Using scanning electron microscopy (SEM), the shape and surface morphology of the optimized formulation of freeze-dried drug-loaded nanoparticles were examined.[51]

4. In-vitro Drug Release Studies: Using the dialysis bag method and the dialysis membrane, in-vitro drug release studies were conducted using pH 7.4 phosphate buffer containing 0.5% v/v Tween 80. 5 mg of medication equivalent in nanoparticle dispersion was then put into the bag for dialysis membranes & sealed at both ends, then stored in a beaker with the contents. A pH 7.4 phosphate buffer solution (100 ml). At 100 rpm, both temperature and speed were maintained. To keep the sink conditions, the samples were taken out at prearranged intervals and a comparable volume was added to the fresh buffer solution at the same time. The samples were examined with a UV-visible spectrophotometer set to 228 nm. The amount of drug released was used to further calculate the cumulative percentage release.[52]

5. Stability Studies: The stability studies of the optimal nanoparticle formulation were carried out by storing it at 30 ºC ± 2 ºC / 65% ± 5% RH for 90 days. The changes in particle size and percentage entrapment efficiency were monitored at regular intervals.[53]

CONCLUSION

Nanotechnology is the most promising scientific topic of our century since it is a new technology. As nanotechnology advances, an increasing number of novel nanomaterials will be created and used in medical care, which will advance the field of modern medicine, generate fresh concepts, and aid in the diagnosis, prevention, and treatment of illnesses. Studies to improve the solubility, permeability, and chemical stability of numerous medications have proliferated as a result of recent developments in nanoparticle-based oral medicine. The top-down method is not appropriate for soft materials and is quite costly. While the top-down approach works well for laboratory experiments, it is not appropriate for large-scale production. The foundation of the bottom-up method is the idea of molecular Bottom-up approaches require atom by atom, molecule by molecule identification, molecule, or by manipulating clusters one by one to create nano-systems. The investigation of various synthesis techniques for using nanoparticles. Literature review work conclude that the nanotechnology has great promise for advancement of modern medicine which is used to cure a wide range of illnesses.

ACKNOWLEDGMENT

The authors are thankful to the Principal and Management of Kamla Nehru College of Pharmacy, Butibori, Nagpur for providing facilities for my research work.

CONFLICT OF INTEREST

The author announced that they have no known competing financial interest or personal relationship that could have appeared to influence the work reported in this paper.

REFERENCES

1. Simos, Y.V., Spyrou, K., Patila, M., Karouta, N., Stamatis, H., Gournis, D., Dounousi, E. and Peschos, D.,. Trends of nanotechnology in type 2 diabetes mellitus treatment. Asian journal of pharmaceutical sciences, 2021; 16(1): 62-76.
2. Saeedi, P., Petersohn, I., Salpea, P., Malanda, B., Karuranga, S., Unwin, N., Colagiuri, S., Guariguata, L., Motala, A.A., Ogurtsova, K. and Shaw, J.E., 2019. Global and regional diabetes prevalence estimates for and projections for 2030 and 2045: Results from the International Diabetes Federation Diabetes Atlas. Diabetes research and clinical practice, 2019; 157: 107843.
3. Diabetes: Mechanism, Pathophysiology and Management-A Review Anees A Siddiqui 1*, Shadab A Siddiqi, Suhail Ahmad, Seemi Siddiqui3, Iftikhar Ahsan1, Kapendra Sahu., 2021; 1: 1-10.
4. Padhi, S., Nayak, A.K. and Behera, A., Type II diabetes mellitus: a review on recent drug-based therapeutics. Biomedicine & Pharmacotherapy, 2020; 131: 110708.
5. Hu, C. and Jia, W., Therapeutic medications against diabetes: what we have and what we expect. Advanced Drug Delivery Reviews, 2019; 139: 3-15.
6. Shaeena, M.H. and Mani, R.K., Diabetes and nanotechnology–A recent advance in treatment of Diabetes. Journal of University of Shanghai for Science and Technology, 2021; 23(11): 445-453.
7. Vieira, R., Souto, S.B., Sánchez-López, E., López Machado, A., Severino, P., Jose, S., Santini, A., Fortuna, A., García, M.L., Silva, A.M. and Souto, E.B., Sugar-lowering drugs for type 2 diabetes mellitus and metabolic syndrome—Review of classical and new compounds: Part-I. Pharmaceuticals, 2019; 12(4): 152.
8. Souto, E.B., Souto, S.B., Campos, J.R., Severino, P., Pashirova, T.N., Zakharova, L.Y., Silva, A.M., Durazzo, A., Lucarini, M., Izzo, A.A. and Santini, A., Nanoparticle delivery systems in the treatment of diabetes complications. Molecules, 2019; 24(23): 4209.
9. Hussain, S. and Chowdhury, T.A., The impact of comorbidities on the pharmacological management of type 2 diabetes mellitus. Drugs, 2019; 79(3): 231-242.
10. Wong, C.Y., Al-Salami, H. and Dass, C.R., Potential of insulin nanoparticle formulations for oral delivery and diabetes treatment. *Journal of controlled release*, 2017; *264:* 247-275
11. Bahman, F., Greish, K. and Taurin, S., Nanotechnology in insulin delivery for management of diabetes. Pharmaceutical nanotechnology, 2019; 7(2): 113-128.
12. Mansoor, S., Kondiah, P.P., Choonara, Y.E. and Pillay, V., Polymer-based nanoparticle strategies for insulin delivery. Polymers, 2019; 11(9): 1380.
13. Mohsen, A.M., Nanotechnology advanced strategies for the management of diabetes mellitus. Current Drug Targets, 2019; 20(10): 995-1007.
14. Nawaz, M.S., Shah, K.U., Khan, T.M., Rehman, A.U., Rashid, H.U., Mahmood, S., Khan, S. and Farrukh, M.J., Evaluation of current trends and recent development in insulin therapy for management of diabetes mellitus. Diabetes & Metabolic Syndrome: Clinical Research & Reviews, 2017; 11: S833-S839.
15. Shah, P., Chavda, K., Vyas, B. and Patel, S., Formulation development of linagliptin solid lipid nanoparticles for oral bioavailability enhancement: Role of P-gp inhibition. Drug delivery and translational research, 2021; 11: 1166-1185.
16. Ghasemiyeh, P. and Mohammadi-Samani, S., Solid lipid nanoparticles and nanostructured lipid carriers as novel drug delivery systems: Applications, advantages and disadvantages. Research in pharmaceutical sciences, 2018; 13(4): 288-303.
17. Begum, M.Y. and Gudipati, P.R., Formulation and evaluation of dasatinib loaded solid lipid nanoparticles. Int. J. Pharm. Pharm. Sci, 2018; 10: 14-20.
18. Xue, J., Wang, T., Hu, Q., Zhou, M. and Luo, Y., A novel and organic solvent-free preparation of solid lipid nanoparticles using natural biopolymers as emulsifier and stabilizer. International journal of pharmaceutics, 2017; 531(1): 59-66.
19. Dikusar, A.I., Globa, P.G., Belevskii, S.S. and Sidel'nikova, S.P., On limiting rate of dimensional electrodeposition at meso-and nanomaterial manufacturing by template synthesis. *Surface Engineering and Applied Electrochemistry*, 2009; *45:* 171-179.
20. Li, J., Wu, Q. and Wu, J., Synthesis of Nanoparticles via Solvothermal and Hydrothermal Methods, 2016; 12.
21. Sivasankaran, S., Sankaranarayanan, S. and Ramakrishnan, S., July. A novel sonochemical synthesis of metal oxides based Bhasmas. In *Materials Science Forum*. Trans Tech Publications Ltd., 2013; 754: 89-97.
22. Ziylan-Yavas, A., Mizukoshi, Y., Maeda, Y. and Ince, N.H., Supporting of pristine TiO2 with noble metals to enhance the oxidation and mineralization of paracetamol by sonolysis and sonophotolysis. *Applied Catalysis B: Environmental*, 2015; *172:* 7-17.
23. Das, S. and Srivasatava, V.C., Synthesis and characterization of ZnO–MgO nanocomposite by co-precipitation method. *Smart Science*, 2016; *4*(4): 190-195.
24. Wang, Y., Arandiyan, H., Scott, J., Bagheri, A., Dai, H. and Amal, R., Recent advances in ordered

meso/macroporous metal oxides for heterogeneous catalysis: a review. *Journal of Materials Chemistry A*, 2017; *5*(19): 8825-8846.
25. Manjula, P., Boppella, R. and Manorama, S.V., A facile and green approach for the controlled synthesis of porous SnO2 nanospheres: application as an efficient photocatalyst and an excellent gas sensing material. *ACS applied materials & interfaces*, 2012; *4*(11): 6252-6260.
26. Vidya, C., Hiremath, S., Chandraprabha, M.N., Antonyraj, M.L., Gopal, I.V., Jain, A. and Bansal, K., Green synthesis of ZnO nanoparticles by Calotropis gigantea. *Int J Curr Eng Technol*, 2013; *1*(1): 118-120.
27. Anjum, R. and Lakshmi, P.K., A review on solid lipid nanoparticles; focus on excipients and formulation techniques. *Int. J. Pharm. Sci. Res*, 2019; *10*(9): 4090-4099.
28. Gupta, S., Kesarla, R., Chotai, N., Misra, A. and Omri, A., 2017. Systematic approach for the formulation and optimization of solid lipid nanoparticles of efavirenz by high pressure homogenization using design of experiments for brain targeting and enhanced bioavailability. *Biomed research international*, *2017*.
29. Kushwaha, A.K., Vuddanda, P.R., Karunanidhi, P., Singh, S.K. and Singh, S., 2013. Development and evaluation of solid lipid nanoparticles of raloxifene hydrochloride for enhanced bioavailability. *BioMed research international*, *2013*.
30. Khare, A., Singh, I., Pawar, P. and Grover, K., 2016. Design and evaluation of voriconazole loaded solid lipid nanoparticles for ophthalmic application. *Journal of drug delivery*, *2016*.
31. Priya, S., Koland, M. and Suchetha, K.N., Formulation and characterization of ropinirole hydrochloride loaded solid lipid nanoparticles. *International Journal of Pharmacy and Pharmaceutical Sciences*, 2015; *7*(9): 85-89.
32. Bagul, U.S., Pisal, V.V., Solanki, N.V. and Karnavat, A., Current status of solid lipid nanoparticles: a review. *Modern Applications of bioequivalence & bioavailability*, 2018; *3*(4): 555617.
33. Satapathy, S., Patro, C.N., Jena, G.K., Patro, C.S. and Sahoo, L., A Focus on Fabrication, Characterization, Stability, Skin Targeting, Patent, Safety and Toxicity of Nanostructured Lipid Carrier. *Journal of pharmaceutical research international*, 2022; 49-76.
34. Nitin, P. and Jasmine, A., Synthesis and characterization of cefixime loaded silver nanoparticles for antibacterial activity against staphylococcus aureus.
35. Veni, D.K. and Gupta, N.V., Development and evaluation of Eudragit coated environmental sensitive solid lipid nanoparticles using central composite design module for enhancement of oral bioavailability of linagliptin. International Journal of Polymeric Materials and Polymeric Biomaterials, 2020; *69*(7): 407-418.
36. Padole, N. and Avari, J., Synthesis of Silver Nanoparticles for Antibacterial Activity against Staphylococcus Aureus and Escherichia Coli. *Asian Journal of Pharmaceutical Research and Development*, 2021; *9*(5): 67-73.
37. Padole, N.N., Synthesis of Silver Nanoparticles for Antibacterial Activity against Staphylococcus Aureus and Escherichia Coli. *Asian Journal of Pharmaceutical Research and Development*, 2022; *10*(2): 29-36.
38. Mohseni, R., ArabSadeghabadi, Z., Ziamajidi, N., Abbasalipourkabir, R. and RezaeiFarimani, A., Oral administration of resveratrol-loaded solid lipid nanoparticle improves insulin resistance through targeting expression of SNARE proteins in adipose and muscle tissue in rats with type 2 diabetes. *Nanoscale research letters*, 2019; *14:* 1-9.
39. Shaveta, S., Singh, J., Afzal, M., Kaur, R., Imam, S.S., Alruwaili, N.K., Alharbi, K.S., Alotaibi, N.H., Alshammari, M.S., Kazmi, I. and Yasir, M., Development of solid lipid nanoparticle as carrier of pioglitazone for amplification of oral efficacy: formulation design optimization, in-vitro characterization and in-vivo biological evaluation. *Journal of Drug Delivery Science and Technology*, 2020; *57:* 101674.
40. Seyam, S., Nordin, N.A. and Alfatama, M., Recent progress of chitosan and chitosan derivatives-based nanoparticles: pharmaceutical perspectives of oral insulin delivery. *Pharmaceuticals*, 2020; *13*(10): 307.
41. Othman, S.I., Alturki, A.M., Abu-Taweel, G.M., Altoom, N.G., Allam, A.A. and Abdelmonem, R., Chitosan for biomedical applications, promising antidiabetic drug delivery system, and new diabetes mellitus treatment based on stem cell. *International Journal of Biological Macromolecules*, 2021; *190*; 417-432.
42. Kumar, D., Gautam, A., Rohatgi, S. and Kundu, P.P., Synthesis of vildagliptin loaded acrylamide-g-psyllium/alginate-based core-shell nanoparticles for diabetes treatment. *International Journal of Biological Macromolecules*, 2022; *218:* 82-93.
43. Niculescu, A.G. and Grumezescu, A.M., Applications of chitosan-alginate-based nanoparticles—An up-to-date review. *Nanomaterials*, 2022; *12*(2): 186.
44. Singh, A., Joshi, N.C. and Ramola, M., Magnesium oxide nanoparticles (MgONps): green synthesis, characterizations and antimicrobial activity. *Research Journal of Pharmacy and Technology*, 2019; *12*(10): 4644-4646.
45. Monika, M. and Prema, K.K., Phytochemical analysis of commercially available Spirulina, their activities and Biosynthesis of Nanoparticles. *Research Journal of Pharmacy and Technology*, 2021; *14*(12): 6189-6193.
46. Abdulazeem, L., Jassani, J. and Al-Sheakh, M.A., Free radical scavenging and antioxidant activity of silver nanoparticles synthesized from Cuminum

cyminum (Cumin) seed extract. *Research Journal of Pharmacy and Technology*, 2021; *14*(8): 4349-4354.
47. Andal, P., Tamilselvy, S. and Priyatharesini, P.I., Green synthesis of silver nanoparticles from carrot. *Research Journal of Pharmacy and Technology*, 2018; *11*(7): 2757-2760.
48. Bakthavachalam, A., Remya, P.N. and Damodharan, N., Review on Solid lipid nanoparticles. *Research Journal of Pharmacy and Technology*, 2020; *13*(9): 4430-4434.
49. Kopparam, M., Kulkarni, S.V. and Shivu, S.N., Development, Characterization and In vitro Evaluation of Donepezil solid Lipid Nanoparticles. *Research Journal of Pharmacy and Technology*, 2020; *13*(7): 3113-3121.
50. Gayathri, V., Nivedha, S., Pujita, V. and Romauld, S.I., Green synthesis of copper nanoparticles using bracts of Musa paradisiaca (Monthan) and study of its antimicrobial and antioxidant activity. *Research Journal of Pharmacy and Technology*, 2020; *13*(2): 781-786.
51. Maheshwari, S., Tiwari, R.K. and Singh, L., Green expertise: Synthesis of Silver nanoparticles for wound healing application an overview. *Research Journal of Pharmacy and Technology*, 2021; *14*(2): 1149-1154.
52. Devi, G.K., Suruthi, P., Veerakumar, R., Vinoth, S., Subbaiya, R. and Chozhavendhan, S., A review on metallic gold and silver nanoparticles. *Research Journal of Pharmacy and Technology*, 2019; *12*(2): 935-943.
53. Dhamane, S.P. and Jagdale, S.C., Development of Rifampicin loaded Chitosan nanoparticles by 32 full Factorial design. *Research Journal of Pharmacy and Technology*, 2020; *13*(6): 2545-2550.