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NEWER APPROACHES IN MANAGEMENT OF BLOOD PRESSURE

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ABSTRACT

Blood pressure is one of the important key factors of human body. As per WHO, worldwide 1.13 billion people have high blood pressure, most (two-thirds) living in low- and middle-income countries. In India the prevalence of hypertension is to be 25% in urban and 10% in rural. In India, above age of 60 years, hypertension is more prevalent in females than males and, regardless of Sex, the older the participants were, the more likely they were to have hypertension. Also, Hypertension, a worldwide epidemic at present, is not a disease in itself rather it is a significant risk factor for serious cardiovascular disorders including myocardial infarction, stroke, heart failure, and peripheral artery disease. However, people do suffer from hypotension and shocks which are life-threatening. High and Low blood pressure can be affected, and it can be sometimes lethal if not taken care of at times. Though numerous drugs acting via different mechanism of action are available in the market as conventional formulations for the treatment of hypertension, but they face substantial challenges regarding their bioavailability, dosing and associated adverse effects which greatly limit their therapeutic efficacies.

Keywords *– Hypertension, Hypotension, Blood Pressure, Novel drug delivery systems, Nanoparticles, Challenges.*

1. INTRODUCTION

Blood Pressure (BP) is the force or pressure that the blood exerts on the walls of blood vessels [1]. Systolic blood pressure (SBP) is the highest pressure in the arteries during systole (Ventricular contraction) and Diastolic blood pressure (DBP) is the lowest pressure in the arteries during diastole (Ventricular relaxation) [2]. When the left ventricle contracts and pushes blood into the aorta there is development of the pressure in the arterial system which is known as Systolic blood pressure (SBP). In adults the normal blood pressure is around 120mmHg or 16kPa. When the heart rest after the ejection of the blood following relaxation of ventricles, there is development of the pressure in the arterial system which is known as Diastolic blood pressure (DBP). In adults the normal blood pressure is around 80mmHg or 11kPa. The instrument used to measure the Arterial Blood Pressure is known as *Sphygmomanometer,* and it is expressed as:

BP=120/80 mmHg or BP=16/11 kPa

Blood pressure depends mainly on two mechanisms; the proper functioning of the Heart and a resistance of blood vessels. The combination effects of neurological and hormonal factors, due to these mechanism blood pressure tends to be high or low.

1.1. Hypotension

When the force of the blood drops below the normal range it is called as Hypotension (low blood pressure), which can cause fainting or dizziness as brain does not receive enough blood i.e., 90/60 mmHg. The various stages of blood pressure are summarized in Table-1.

Table-1: Blood pressure stages

Stages	Systolic (mmHg)	Diastolic (mmHg)
Normal blood pressure	Less than 120	Less than 80
Elevated	Between 120 and 129	Less than 80
Stage 1 hypertension	Between 130 and 139	Between 80 and 89
Stage 2 hypertension	At least 140	At least 90
Hypertensive crisis	Over 180	Over 120

Types

Orthostatic or postural hypotension, neutrally mediated hypotension, post-prandial hypotension, Multiple system atrophy with orthostatic hypotension.

Causes / Factors

Pregnancy, Heart disease, Eating disorder, Dietary deficiencies, Hormonal problems, Dehydration, Blood loss, Severe infection (septicaemia), Severe allergy reaction (anaphylaxis), Age, Medications, Certain diseases [3].

Hypotension and shock

Severe hypotension leads to hypotensive shock. Different ways of describing shock depending upon cause [3].

Cardiogenic shock, Distributive shock, Obstructive shock, Hypovolemic shock.

1.2. Hypertension

When the force of the blood against the wall of arteries is too high it leads to Hypertension (high blood pressure) i.e. 140/90 mmHg and in severe cases it is around 180/120 mmHg.

Types

There are two types of hypertensions

- Primary hypertension
- Secondary hypertension

Symptoms

Hypertension is generally a silent condition. Symptoms may include sweating, anxiety, sleeping problems, and blushing, headaches, shortness of breath, nosebleeds, flushing, dizziness, chest pain, blurred vision, blood in the urine.

Pathophysiology

The pathophysiology of hypertension involves the impairment of renal pressure natriuresis, the feedback system in which high blood pressure induces an increase in sodium and water excretion by the kidney that leads to a reduction of the blood pressure.

Pressure natriuresis can result from impaired renal function, inappropriate activation of hormones that regulate salt and water excretion by the kidney (as those in the renin-angiotensin-aldosterone system), or excessive activation of the sympathetic nervous system.

Causes / Factors

Age, Alcohol, Using tobacco, Family history, Sodium in diet, Potassium in diet, Lack of physically active, Stress, Certain chronic conditions.

2. DIAGNOSIS

Blood pressure is measured using a blood pressure cuff, which is a non-invasive device that can detect the pressure inside the arteries, conveying numerical values using a sphygmomanometer or an electronic device. Doctor may also use lab tests or imaging tests to diagnose some of the cause or complications of hypertension [4]. There are two main types of blood pressure (BP) monitors: aneroid and digital. Some models measure BP at the wrist or finger, but there's evidence that they aren't as accurate. Aneroid monitors have a cuff that's inflated by squeezing a rubber bulb, a dial gauge with a needle, and a stethoscope

A sphygmomanometer has three parts:

- a cuff that can be inflated with air,
- a pressure meter (manometer) for measuring air pressure in the cuff, and
- a stethoscope for listening to the sound the blood makes as it flows through the brachial artery (the major artery found in your upper arm). Fig.1.

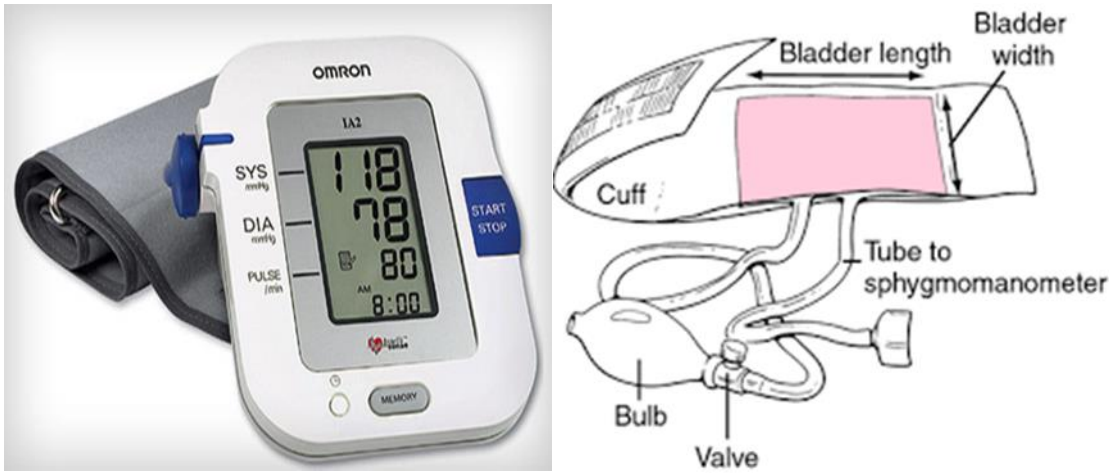

Fig. 1: Digital blood pressure monitor and A Sphygmomanometer

Labs Tests

Blood pressure Tests

Traditionally, blood pressure is measured by using sphygmomanometer. It is an electronic reading device, which is compressed to squeeze and release an external pressure on an artery in arms, measuring maximum pressure when heart beats (systolic) and lowest pressure when heart relaxed (diastolic).

Measuring resting Blood pressure

This is usually done in a quiet and warm environment so that the patient sits at least for 5 minutes with feet supported to ground so as to avoid any errors in the measuring of blood pressure. The patients who have elevated blood pressure in the office or clinic due to anxiety, but have normal blood pressure at home are known as *White coat hypertension.*

Blood tests

Blood testing is not diagnostic for hypertension, but tests are frequently ordered to detect conditions that may cause or make high blood pressure worse and to evaluate and monitor organ function over time. Blood tests that may be ordered to assist in the diagnosis of hypertension include: Electrolyte levels, Blood glucose, Thyroid function tests, Kidney function tests.

Urine Tests

General test that may be ordered include: Urinalysis, urine protein, Urinary albumin (microalbumin), BUN (blood urea nitrogen), creatinine, estimated glomerular filtration rate (eGFR), Potassium, Calcium.

Self-Checks/At-Home Testing

Home Blood Pressure Monitoring (HBPM)

Home blood pressure monitors are accurate and easy to use. It is one of the viable options for diagnosing hypertension and helping manage it once identified. This method is particularly helpful for those who are suffering from White Coat Hypertension. Medical devices are available for HBPM.

Ambulatory Blood Pressure Monitoring (ABPM)

Ambulatory Blood Pressure Monitoring (ABPM) measures blood pressure at regular intervals. It is believed to be able to reduce the white coat hypertension effect in which a patient's blood pressure is elevated during the examination process due to nervousness and anxiety caused by being in clinical setting. ABPM can also detect the reverse condition, masked hypertension, where the patients have normal blood pressure during the examination but uncontrolled blood pressure at home. An ABPM device consists of a blood pressure cuff that is worn on the arm and attached to a recording device, which can be worn on a belt [4].

Imaging Techniques

Imaging techniques allows a comprehensive assessment of patients with suspected hypertension. It plays a key part in the initial diagnostic and prognostic assessment and machine learning approaches show promise in the diagnosis of hypertension. They are Electrocardiogram (EKG), Echocardiogram, Ultrasound, CT scan or MRI.

Differential Diagnosis

A differential diagnosis is a list of possible conditions or diseases that could be causing the symptoms; it is based off of the facts obtained from the symptoms, medical history, basic laboratory results, and a physical examination.

3. TREATMENT

3.1. Treatment for hypotension

Low blood pressure that either doesn't cause signs or symptoms or causes only mild symptoms rarely requires treatment. Depending on age, health and the type of low blood pressure patient have, the several ways of treatment are;

- **Use of more salt, Drinking more water, Medications.**

- **Wearing compression stockings.** Compression stockings are elastic compression garments worn around the leg, compressing the limb. The elastic stockings commonly used to relieve the pain and swelling of varicose veins can help reduce the pooling of blood from the legs.
- **Lifestyle and home remedies:** Drinking more water and less alcohol, paying attention on body positions, Eat small low-carb meals, Exercise regularly.

3.2. Treatment for hypertension

Antihypertensive drug

Most of these drugs possess some significant drawbacks like low bioavailability, relatively short half-life, low permeability, and adverse side effects. For effective delivery of these antihypertensive drugs, such drug delivery systems are needed which can provide the following characteristics: (1) low dosing frequency, (2) enhanced bioavailability, (3) increased selectivity, and (4) reduced side effects. The classification of antihypertensive drug is depicted in Fig.2.

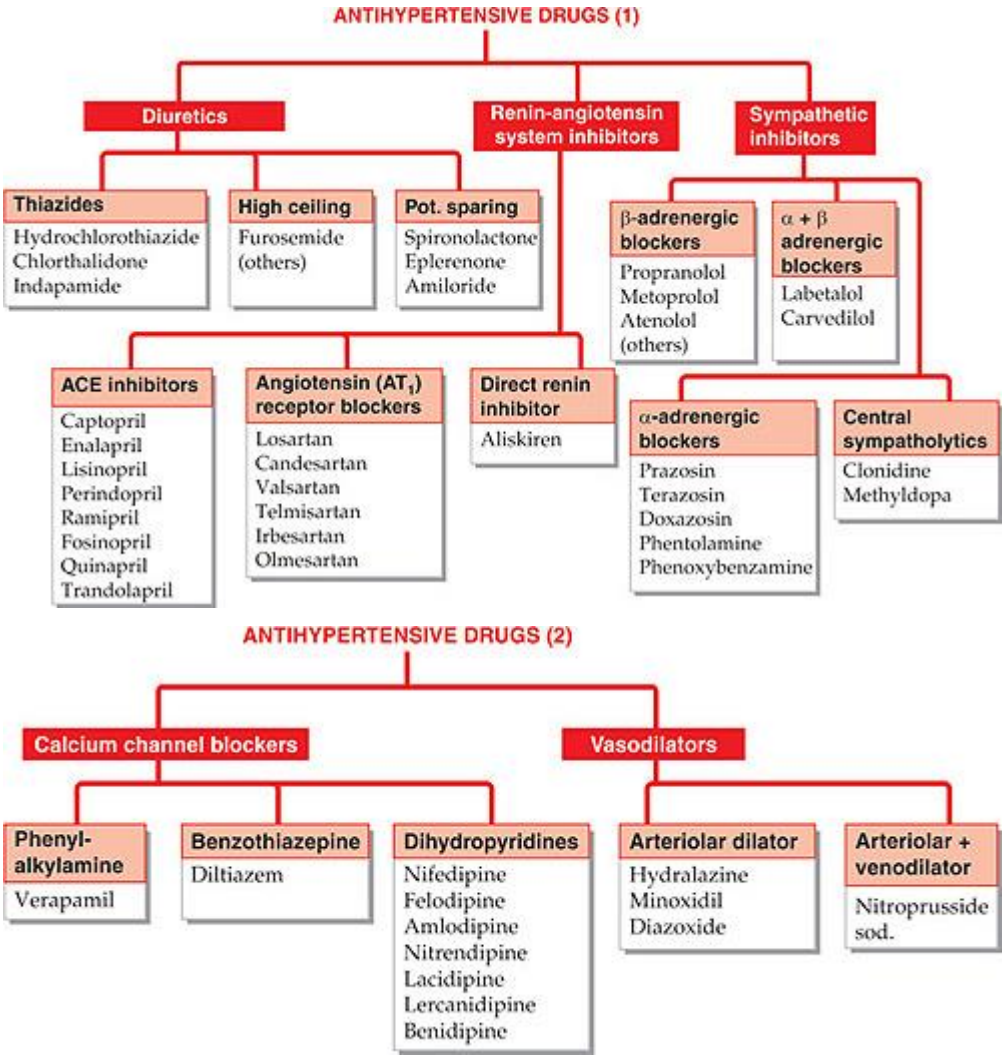

Fig.2: Classification of Anti-hypertensive agents

4. CHALLENGES IN ORAL DRUG DELIVERY

Oral drug delivery is the most common, convenient, and extensively used route of administration as it offers advantages like painless administration, no assistance, and patient compliance as compared to other routes such as intramuscular, intravenous, and pulmonary. However, several compounds are unsuccessful and fail in research and development owing to their low absorption and low bioavailability upon oral administration. The drugs with poor oral bioavailability are unable to reach the minimum effective concentration to exhibit therapeutic action. Some of the reasons for poor bioavailability are as follows:

- One of the reasons is poor solubility of drugs that affects the bioavailability as drug should be present in solution form at absorption site.
- Another is inappropriate partition coefficient as it influences the permeation of drug through lipid membrane.
- First-pass metabolism causes metabolism of drug which results in poor absorption and low bioavailability of the drugs.
- P-glycoprotein (P-gp) mediated efflux also was shown to alter the pharmacokinetics of drug; the presence of P-glycoprotein in the liver, kidney, and intestine causes reduction in absorption of drug from the gastrointestinal tract and increase in drug elimination; an antihypertensive drug, talinolol, is a P-gp substrate whose oral bioavailability is limited by P-glycoprotein mediated efflux. Certain antihypertensive like Deltiazem, Nicardipine, and Nifedipine are the candidate for the P-glycoprotein (P-gp)-mediated efflux transporter present in the intestinal wall apart from Cytochrome P450-mediated enzymatic metabolism.
- Degradation of drug in the gastrointestinal tract due to pH of the stomach or enzymatic degradation or by chemical reactions also alters oral bioavailability of drugs.

5. NANOCARRIERS AS TREATMENT MODALITIES FOR HYPERTENSION

Various studies have demonstrated that nanocarriers can significantly increase the drug bioavailability thereby reducing the frequency of dosing in addition to minimizing toxicity associated with high dose of the drug. Hypertension has circadian pattern of blood pressure, therefore chronotherapeutics can play a decisive role for the treatment, and however, nanoparticulate system can play major role in hypertension management. Future prospective for particulate nanocarriers in drug delivery for hypertension includes chronotherapeutics and emerging technique like gene therapy [5]. Hindrance in the oral absorption of the drugs includes extreme pH, poor intestinal permeability, and CYP 450-mediated enzymatic metabolism. Incorporation of the drug into nanoparticles can overcome these barriers [6]. Nanoparticles have been reported which increase the uptake of drug through different mechanism which includes transcellular absorption, Paracellular transport by opening tight junction, P-gp inhibition, inhibition of gut wall metabolism by CYP450, and enhancement of lymphatic transport [7]. Nanoparticles of size 100 nm have been considered ideal for lymphatic transport of lipid nanoparticle [8]. Solutol HS 15, poloxamer 188, polyethylene glycol, and Cremophor RH 40 are some surfactants used in formulating nanoparticles and show inhibition of P-gp efflux and CYP450 activity [9]. Most of the antihypertensive drug comes under BCS class 2 (low solubility and high permeability) which have low bioavailability as dissolution is the rate-limiting step. Drugs like Amlodipine and Isradipine apart from having low bioavailability are also light sensitive apart from being a BCS class 2 drugs. Delivery of such drug in protected form is required to prevent their photo-degradation. Both drugs were delivered by utilizing nano emulsion as a drug delivery system. Their pharmacokinetic data revealed the stability and enhanced bioavailability [10,11]. Chronotherapeutics can deliver drugs at the time when symptoms occur like during night and early morning as in the case with hypertension. Gene silencing is the recent technology where the use of small interfering RNA is done to silence those receptors which are involved in the increase of blood pressure [5]. Intravenous route is mostly used for the delivery of SiRNA in treating hypertension. Incorporation of SiRNA in delivery system is required to prevent

their degradation by exonuclease activity present in blood [12,13]. Oral delivery has been rarely studied for the delivery of SiRNA for the treatment of hypertension. Summary of the investigations some nano systems of Antihypertensive drugs is provided in Table-2.

Table-2: Summary of the investigations some nano systems of Antihypertensive drugs

Name of drug	Colloidal system	Applications
Carvedilol	Solid lipid nanoparticles	Enhanced bioavailability and protecting it from acidic environment
	Nano suspensions	Increased oral bioavailability
	Carbon nanotubes	Drug loading capacity and improving the solubility
	Mesoporous silica nanoparticles	Improvement in drug loading and drug release profile
Nebivolol	Polymeric nanoparticles	Prolonged drug release
Valsartan	Solid lipid nanoparticles	Bypassing first-pass metabolism, enhancing lymphatic absorption, and improving solubility and bioavailability
	Nano suspensions	Enhanced drug release
	Self-Nano emulsifying drug delivery system	Increase in dissolution rate
	Polymeric nanoparticles	Prolonged release of drug and thereby it decreases its dose size, frequency of dose, and side effects
	Proliposomes	Good flowability and particle size distribution and well conversion into liposomes by hydration and desirable in vitro drug release
Felodipine	Nano suspensions	Enhanced solubility and oral bioavailability
	Polymeric nanoparticles	Controllable drug release and effective in vitro compatibility
Nifedipine	Dendrimers	Enhanced water solubility
	Polymeric nanoparticles	Enhanced oral bioavailability
	Nanocrystals	Enhanced dissolution rate
Candesartan cilexetil	Dendrimers	Improved water solubility
	Nano suspensions	Improved bioavailability
	Polymeric micelles	Increased drug loading capacity and drug release
Nitrendipine	Solid lipid nanoparticles	Enhanced bioavailability
	Nano emulsions	Improved therapeutic efficacy and bioavailability
	Nanocrystals	Improvement in physical stability, in vitro drug release, and bioavailability

6. CURRENTLY USED NANO CARRIERS FOR THE ANTIHYPERTENSIVE DRUG DELIVERY

6.1. Solid Lipid Nanoparticles (SLNs)

Lipid nanocarriers have gained significant attention in oral drug delivery in the last few decades. The SLNs (Fig. 3) are submicron colloidal carrier which is composed of physiological lipid, dispersed in water or in an aqueous surfactant solution [14]. SLNs offer benefits such as biocompatibility, nontoxicity, and stability against coalescence. Solid lipid nanoparticles can be applied for delivery of hydrophilic as well as hydrophobic drugs [15,16]. Venishetty et al. have shown solid lipid nanoparticles (SLNs) containing carvedilol as a promising strategy to enhance the bioavailability of such poorly soluble drugs. They prepared carboxymethyl chitosan (MCC) coated carvedilol loaded SLNs to improve its bioavailability and to protect it from acidic environment [17].

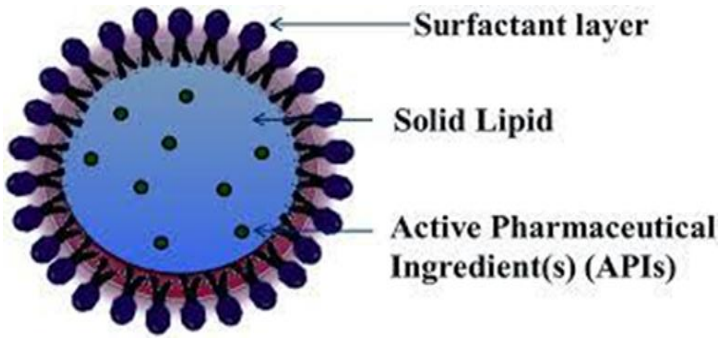

Fig. 3: Solid Lipid Nanoparticles

6.2. Dendrimers

Dendrimers (Fig. 4) are innovative polymeric carrier attracting attention due to their advantages that include three-dimensional structure, nanometer size, narrow polydispersity index, and controlled molecular structure and are also accompanied with multiple functional groups/multivalency. The word “dendrimers” is derived from a Greek word “Dendra,” which means reminiscent of a tree [18]. Dendrimers have size ranging between 1 and 100 nm with three distinct domains: (i) a core, which is at the center containing atom or a molecule with at least two identical chemical functions; (ii) branches, which are the units repeated in geometric progression that leads to radially concentric layers known as “generations”; and (iii) terminal functional groups, at the surface which determines the properties of dendrimers.

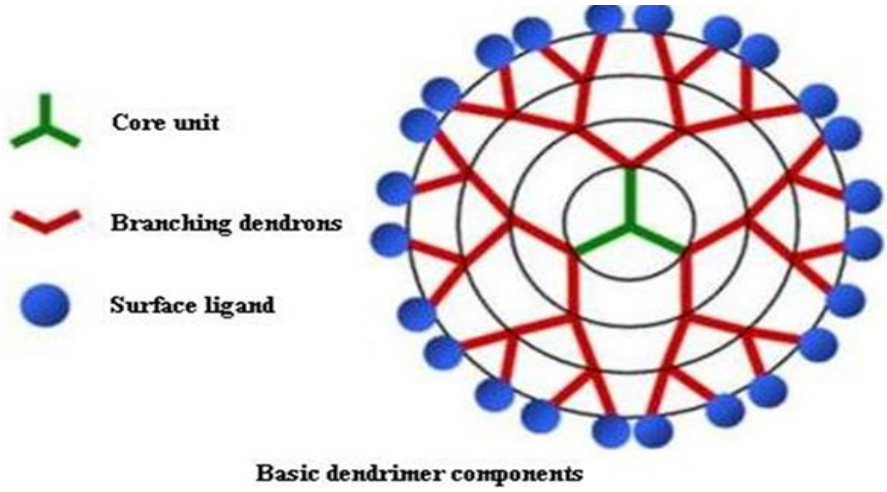

Fig.4: Dendrimer

Different types of dendrimers are available on the basis of different polymers such as polyamidoamines (PAMAMs), polyamines, polyamides (polypeptides), poly(aryl ethers), polyesters, carbohydrates, and DNA. PAMAM dendrimers are most commonly used. Candesartan cilexetil is a calcium channel blocker used in the treatment of hypertension. The permeability of candesartan cilexetil depends on its aqueous solubility and lipid-protein partition coefficient in relation to the stratum corneum. In an investigation, Gautam and Verma fabricated polyamidoamine (PAMAM) dendrimers containing candesartan cilexetil. The results of investigation have showed significant increase in water solubility of candesartan cilexetil in the form of PAMAM dendrimers [19].

6.3. Nanosuspensions

Nanosuspensions can overcome the problems related to the delivery of poorly water-soluble drugs due to their nanosize particle range. Nanosuspensions can be formulated with high solid content up to 40%, which reduces their dose size and improves patient compliance. Various methods such as spray drying, freeze drying, and extrusion-spheronization have been applied for converting nanosuspensions to pellets/tablet-like dosage forms. Patel et al. have described an approach to develop a nanosuspension of a poorly water-soluble antihypertensive drug to improve the bioavailability. Further, the optimized batch of nanosuspension was converted into a solid dosage form. Telmisartan (TLM) was selected as a model drug. The TLM loaded nanosuspension was optimized by applying 32 full factorial design. The concentration of stabilizer and amount of milling agents were taken as principal component of analysis (PCA). Lyophilization process was used to develop tablets of nanosuspension. The *in vitro* drug release study was carried out over optimized batch of TLM loaded tablets, marketed tablets (Sartel® 20), and conventional tablets in 0.1 M HCl as a dissolution medium. The results of *in vitro* drug release have demonstrated higher value of cumulative percentage release (CPR) for nanosuspension loaded tablet formulation in comparison to two other formulations [20]. The *in vivo* pharmacokinetic study was performed in TLM loaded tablets against marketed tablets in Wistar rats and also revealed improvement in rate of absorption from nanosuspension. Thus, the study indicated improvement in rate and extent of oral absorption of TLM from nanosuspension loaded tablets as compared to marketed formulations. This effectiveness was attributed to nanometer size of particles in nanosuspension with subsequent increase in surface area and absorption. The other properties of nanosuspensions like rapid onset of action, enhanced surface area, higher level of saturation solubility, and higher adhesiveness to gastrointestinal epithelium also led to improved oral absorption and bioavailability of lipophilic drugs. The steps involved in the preparation of nanosuspension are represented in Fig.5.

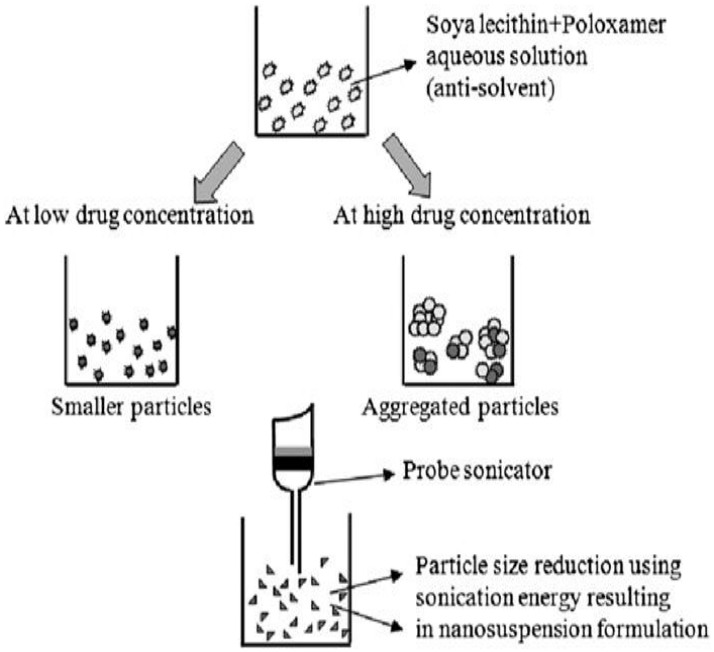

Fig. 5: Nano suspension Formulation

6.4. Nanoemulsions

Nanoemulsions (Fig. 6) are oil-in-water (o/w) emulsions with droplet size in the range of 100 and 500 nm. Nanoemulsions provide advantages of solubilization of hydrophobic molecules in the oily phase, modification of oil droplets with polymers to prolong circulation time, and targeting tumors passively and/or targeting ligands actively. Most commonly used methods to prepare nanoemulsions are low-energy emulsification and high-energy emulsification [21]. Ghai and Sinha have developed nanoemulsions as emulsified drug delivering carrier for selective *β*-1 adrenoreceptor blocker of talinolol. The talinolol nanoemulsion is comprised of 5% (w/v) Brij-721 ethanolic solution, triacetin, and water in ratio of 40: 20 : 40 (%w/w). The droplet size, polydispersity index, surface morphology, and *in vitro* and *in vivo* release of nanoemulsion were investigated. The results of the study have revealed significant increase in drug release and bioavailability, which showed increase in solubility of drug from nanosized emulsion [22].

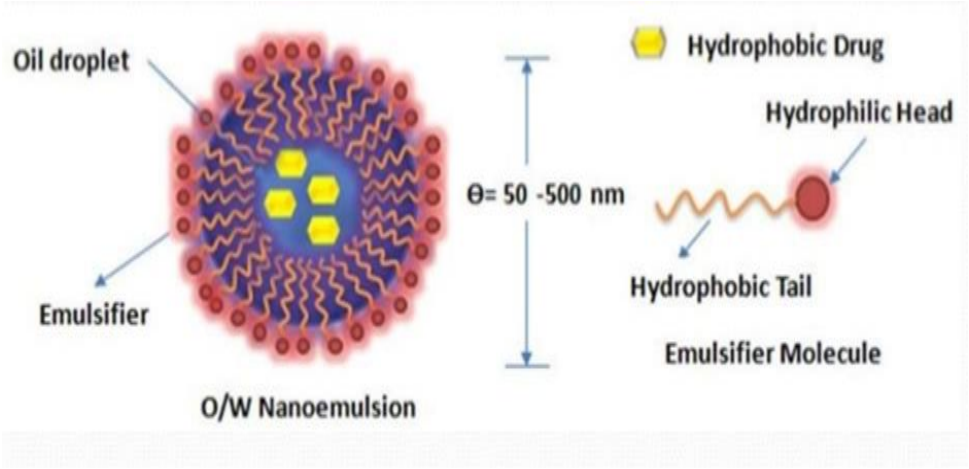

Fig. 6: Nano emulsion

6.5. Self-Nanoemulsifying Drug Delivery System (SNEDDS)

SNEDDS (Fig. 7) are nanoscale oil-in-water (O/W) nano emulsion, available in the form of anhydrous isotropic mixture of surfactant, oil, and drug, which when introduced into aqueous phase with gentle agitation get converted into nano emulsion. The digestive motility of gastrointestinal tract provides required agitation for formation of nanoscale emulsions. The SNEDDS retain benefits associated with nano emulsions like increased oral bioavailability, increased permeation of drug, improved chemical and enzymatic stability, and ease of fabrication and scale-up. The SNEDDS of poorly water-soluble drug have shown improvement in solubility. Rajinikanth et al. have shown significant increase in dissolution rate of valsartan by forming its SNEDDS. The SNEDDS of valsartan was developed using Labrasol (oil), Tween 20, and PEG 400. The investigation data showed desirable zeta potential, stability, droplet size, and sixfold increase in drug release as compared to marketed valsartan tablet and powder. From the results, it may be concluded that SNEDDS of poorly soluble drugs presents a promising drug formulation system for oral delivery of antihypertensive drugs [23].

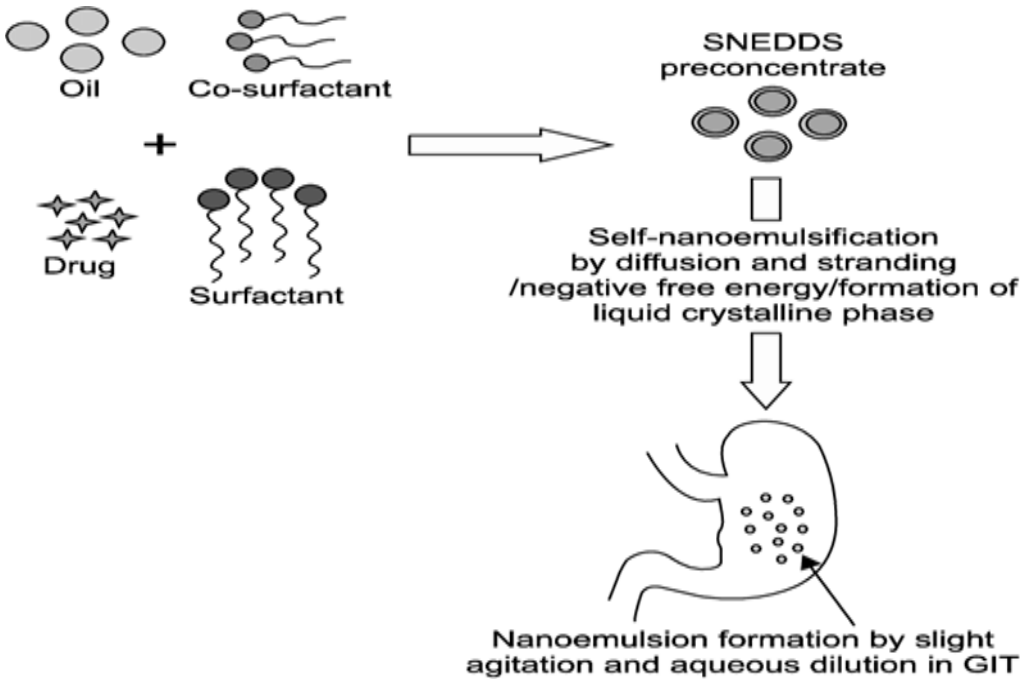

Fig. 7: Self-Nanoemulsifying Drug Delivery System (SNEDDS)

6.6. Polymeric nanoparticles

Polymeric nanoparticles (Fig. 8) are colloidal drug delivery carriers with particle size of 10 to 100 nm. The main advantages of nanoparticles are (1) enhanced bioavailability, (2) increased specificity and targeting to desired site, and (3) reduced toxicity and dose. All these benefits enable safe delivery of drugs specially to target sites without affecting normal tissue. These nanoparticles are prepared by employing biodegradable, synthetic, and natural polymers. The therapeutic effect of polymeric nanoparticles significantly depends on drug release and biodegradation of polymers. The drug release from nanoparticles follows diffusion mechanism, erosion mechanism, or both erosion and diffusion in combination [24]. Jana et al. have studied nanoparticles of nebivolol by employing Eudragit RS 100. The nanoparticles were developed by solvent evaporation process. The polymeric nanoparticles have shown increase in antihypertensive activity owing to its improved oral bioavailability and long-lasting action [25].

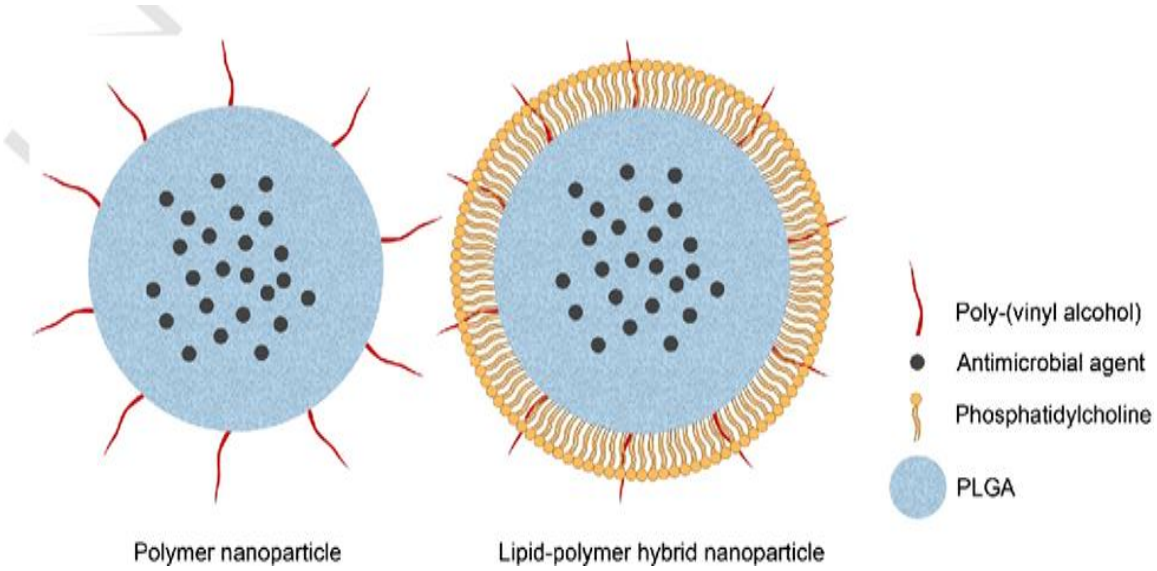

Fig. 8: Polymeric Nanoparticles

6.7. Carbon Nanotubes (CNTs)

Presently, carbon nanotubes are gaining tremendous attention as novel drug delivery carriers. CNTs offer features like (1) high cellular uptake, (2) enhanced trans membrane penetration accumulation due to needlelike shape of CNTs, and (3) ability of high drug loading owing to their increased surface area. Several *in vivo* and *in vitro* studies on CNTs have proven them to be an effective drug delivery system. The poly(amidoamine)- (PAMAM-) functionalized multiwalled carbon nanotubes (MWNTs) loaded with poorly water-soluble carvedilol were developed to improve the drug loading capacity and dissolution.

6.8. Nanocrystals

Nanocrystals are comprised of aggregates of large number of atoms with size between 10 nm and 400 nm. The steps involved in formation of nanocrystals involve formation of nanosuspension, followed by wet milling, high pressure homogenisation, nanocrystallisation, and finally spray drying to obtain nanosized crystals [26]. The decrease in drug particle size to nanoscopic crystals results in an increased surface area to volume ratio [27].

6.9. Proliposomes

Proliposomes are defined as dry, free-flowing particles with a dispersed system that can immediately form a liposomal suspension when in contact with water. Compared with conventional liposomes, proliposomes exhibit more advantages in promoting drug absorption. Because of their solid properties, the physical stability of liposomes can be improved without influencing their intrinsic characteristics. Therefore, proliposomes would be a potential vehicle to help improve the oral absorption of hydrophobic drugs [28,29]. Isradipine-loaded proliposomes were developed to enhance the oral bioavailability and were compared with its oral suspension.

7. CONCLUSION

Nanotechnology holds a great potential in effective delivery of poorly soluble antihypertensive drugs by improving solubility and oral bioavailability. Moreover, novel drug delivery approaches have appeared as strategies to revitalize the development of new hydrophobic entities. The biocompatibility, colloidal size, drug targeting, lowered dose size, reduced toxicity, and patient compliance are some important advantages of nano systems. Although significant advancements are made in nanotechnology, some challenges have been encountered in the development of novel drug delivery systems like (a) transformation of these nanocarrier systems from laboratory scale to pharmaceutical market, (b) depending on factors like cost of fabrication, reproducibility of properties of formulation on production scale, and (c) benefits to human population owing to large variation in pharmacokinetics. However, despite these challenges, the development and benefits offered by novel drug delivery systems cannot be ignored. Thus, nanotechnology offers opportunity for formulation scientists to extend research and development to overcome the challenges related with current antihypertensive drugs, thereby improving the patient compliance and therapeutic efficacy.

8. DISCLOSURE OF CONFLICT OF INTEREST

The author declares no conflict of interest.

REFERENCES

1. Anne Waugh and Allison Grant, Ross and Wilson Anatomy and Physiology in Health and Illness, 12th edition.
2. Gerard J. Tortora, Bryan Derrickson, Principles of Anatomy and Physiology, 14th edition, Bergen Community College, Valencia College, WILEY.

3. Debra Sullivan, Yvette Brazier, Low Blood Pressure (Hypotension), 2020.
4. Richard N., Ali Y. S., How Hypertension Is Diagnosed, 2020.
5. Alam T., Khan S., et.al, Nanocarriers as treatment modalities for hypertension, Drug Delivery, 2017, 24:1, 358-369.
6. Pridgen EM, Alexis F, et.al, Polymeric nanoparticle technologies for oral drug delivery, Clin Gastroenterol Hepatol, 2014, 12:1605–10.
7. Hauss DJ, Oral lipid-based formulations, Adv Drug Deliv, 2007, Rev 59:667,76.
8. Ghosh S, Roy T., Nanoparticulate drug-delivery systems: lymphatic uptake and its gastrointestinal applications, JAPS, 2014, 4:123–30.
9. Khan S, Baboots S, et.al, Immunosuppressive drug therapy-biopharmaceutical challenges and remedies, Expert Opin Drug Deliv, 2015, 12:1333–49.
10. Jang D-J, Jeong EJ, et al., Improvement of bioavailability and photostability of amlodipine using redispersible dry emulsion, Eur J Pharm Sci, 2006, 28:405–11.
11. Havanoor SM, Manjunath K, et al., Isradipine loaded solid lipid nanoparticles for better treatment of hypertension – preparation, characterization and in vivo evaluation, Int J Biopharm, 2014, 5:218–24.
12. Nolte A, Schneider M, et al., Gene-silencing for treatment of cardiovascular diseases. In Eberli D, ed. Regenerative medicine and tissue engineering - cells and biomaterials. Rijeka, Croatia: INTECH 2011.
13. McLendon JM, Joshi SR, et al., Lipid nanoparticle delivery of a microRNA-145 inhibitor improves experimental pulmonary hypertension, J Control Release, 2015, 210:67–75.
14. Mukherjee S., Ray S., et.al, "Solid lipid nanoparticles: a modern formulation approach in drug delivery system," Indian Journal of Pharmaceutical Sciences, 2009, 71(4), 349–358.
15. Müller R. H., Mäder K., et.al, "Solid lipid nanoparticles (SLN) for controlled drug delivery—a review of the state of the art," European Journal of Pharmaceutics and Biopharmaceutics, 2000, 50(1), 161–177.
16. Ramteke K. H., Joshi S. A. et.al, "Solid lipid nanoparticle: a review," IOSR Journal of Pharmacy,2012, 2(6), 34–44.
17. Venishetty V. K., Chede R., et.al, "Design and evaluation of polymer coated carvedilol loaded solid lipid nanoparticles to improve the oral bioavailability: a novel strategy to avoid intraduodenal administration," Colloids and Surfaces B: Biointerfaces, 2012, 95, 1–9.
18. Kaur M., "Dendrimers: synthesis, its dosage forms and advantage over linear polymers," Mintage Journal of Pharmaceutical & Medical Sciences, 2014, 3(3), 15–19.
19. Gautam S. P., Verma A., "PAMAM dendrimers: novel polymeric nanoarchitectures for solubility enhancement of candesartan cilexetil," Pharmaceutical Sciences, 2012,1, 1–4.
20. Patel J., Dhingani A., et.al, "Design and development of solid nanoparticulate dosage forms of telmisartan for bioavailability enhancement by integration of experimental design and principal component analysis," Powder Technology, 2014,258, 331–343.
21. Solans C., Solé I., "Nano-emulsions: formation by low-energy methods," Current Opinion in Colloid & Interface Science, 2012, 17(5), 246–254.
22. Ghai D., Sinha V. R., "Nanoemulsions as self-emulsified drug delivery carriers for enhanced permeability of the poorly water-soluble selective β1-adrenoreceptor blocker Talinolol," Nanomedicine: Nanotechnology, Biology, and Medicine, 2012, 8(5), 618–626.

23. Rajinikanth P. S., Keat N. W., et.al, "Self-nanoemulsifying drug delivery systems of Valsartan: preparation and in-vitro characterization," International Journal of Drug Delivery, 2012, 4, 153–163.
24. Mudshinge S. R., Deore A. B., et.al, "Nanoparticles: emerging carriers for drug delivery," Saudi Pharmaceutical Journal, 2011,19(3), 129–141.
25. Ochekpe N. A., Olorunfemi P. O.,et.al, "Nanotechnology and drug delivery part 2: nanostructures for drug delivery," Tropical Journal of Pharmaceutical Research, 2009, 8 (3), 275–287.
26. Kim Y. I., Fluckiger L., et.al, "The antihypertensive effect of orally administered nifedipine-loaded nanoparticles in spontaneously hypertensive rats," British Journal of Pharmacology, 1997,120(3), 399–404.
27. Arzani G., Haeri A., et.al, "Niosomal carriers enhance oral bioavailability of carvedilol: effects of bile salt-enriched vesicles and carrier surface charge," International Journal of Nanomedicine, 2015,10, 4797–4813.
28. Junyaprasert V. B., Morakul B., "Nanocrystals for enhancement of oral bioavailability of poorly water-soluble drugs," Asian Journal of Pharmaceutical Sciences, 2015, 10(1), 13–23.
29. Hildebrand, Beyer K., et.al, "Temperature dependence of the interaction of cholate and deoxycholate with fluid model membranes and their solubilization into mixed micelles," Colloids and Surfaces B: Biointerfaces, 2003,32(4), 335–351.