Review Article

Advances of Nanotechnology for Improvement of Oral Bioavailability of Antihypertensive Drugs

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ABSTRACT

Conventional route of drug administration is contemplate supported the on the location at which drug is applied. It concerned oral intravenous, ophthalmic etc. Among them oral route of drug administration is the most convenient route of drug delivery because it extends high patient compliance. At an equivalent time, poor metabolic stability and therefore poor liquid solubility of medication are major disadvantages in oral drug delivery. There are various approaches to beat the issue associated with poor aqueous soluble drugs. Among many approaches nanotechnology has gained potential to beat this among challenges mainly associated with Conventional route of administration. The application of these nanotechnology based systems in the treatment of hypertension goes forward. Nanotechnology has gained inflated attention for delivering therapeutic agents effectively to the circulatory system. Heart targeted nano carrier primarily based drug delivery may be a new, effective and efficacious approach for treating numerous internal organ connected disorders like induration of the arteries, cardiovascular disease, and infarct. Nano carrier primarily based drug delivery system circumvents the issues related to standard drug delivery systems, together with their no specificity, severe aspect effects and injury to the conventional cells. Modification of chemical science properties of Nano carriers like size, form and surface modifications will vastly alter its *in vivo* pharmacokinetic and pharmacodynamics information and can offer higher treatment strategy. Many nano carriers like super molecule, lipoid nanoparticles are developed for delivering medicine to the target sites among the center. This review summarizes and will increase the understanding of the advanced nano sized drug delivery systems for treating vessel disorders with the promising use of engineering science. The present review focuses on varied Nano carriers offered in oral drug administration for rising solubility profile, dissolution, and consequently bioavailability of hydrophobic medication drugs.

Keywords: Hypertension; Chronotherapeutics; Lipoid nanoparticle

INTRODUCTION

Nanotechnology including the nanoparticles, nanomaterial and nanostructures has becoming a most priority field for technological development as well as scientific research. The utilization of nanotechnology has already had a multiple applications in electronics, magnetic separation and preconcentration of target analyses and targeted drug delivery as well as in the other fields like vehicles for gene and drug delivery also. At the same time the greatest prospects are its utilization in the field of health and biotechnology with the aim of direct impact on the quality of health in societies. The issuing of nano medicine contributes medicine and nanotechnology together in order to formulate the novel therapies for improving the existing treatments. The nanoparticles are classically according to size and the size range are 1 nm–100 nm, but it is frequently covered just the below range of 1 μm in size. These novel properties of nanoparticle make the nanotechnology excellent for the applications in the biomedical field. Nanotechnology is a very novel field of science that has contributed to modern approaches in many areas of medicine. Now it is also possible to provide a molecular level therapy with the help of nanotechnology and treating diseases etc.

High blood pressure or hypertension withal called as the mute killer because it has no macrocosmic symptoms till no earnest

complications arise. Hypertension is a most prevalent health quandary in today's date. Blood pressure is higher in blood vessels than in the venous system which is proximate to the heart. BP is more in arterial system because the arteries walls are thicker than the walls of the veins. Many cardiovascular complications are directly cognate with blood pressure. Like heart failure, stroke, angina, myocardial infarction, kidney failure [1]. Hypertension or high vital sign is outlined as having a pulsation vital sign (SBP)>140 mmHg or a pulse vital sign (DBP)>90 mmHg. Consistent with the globe health organization, geneva, in 2008, high vital sign junction rectifier to a forty five death rate from anaemia cardiovascular disease and a fifty one death rate from stroke. In 1980, 600 million individuals had high vital sign whereas in 2008 this graph was raised to 1 billion that raised nice concern to manage this condition effectively (WHO, 2013).

Several medicines in standard indefinite quantity forms square measure offered to treat high blood pressure however majority of the medicine square measure poorly water soluble and thus exhibit low bioavailability. These medicines are substrate of Pgp and exhibit vital first-pass metabolism. The opposite challenges with these formulations square measure their short half-life and high dosing frequency. With the employment of extended unharness systems, these dosing frequencies are often reduced however as so much as sweetening of bioavailability cares nanoparticles square measure much better approach. The associated advantages with nanoparticle embody their capability of circumventing first-pass metabolism; Pgp mediate outflow and achieving targeting as a result of entrapped drug in carrier is directly taken into the circulation. A complication within the oral absorption of the drug admits dynamical hydrogen ion concentration, inadequate enteric permeableness and inadequate accelerator metabolism. However nanoparticles incorporation with drug will defeat those complication mentioned within the higher than Proteins and peptides medicine together with internal secretion glargine, etanercept, cyclosporine, desmopressin, and jellyfish scleroprotein supermolecule (have medication movement) square measure poorlybioavailable owing to their charged nature, high sub-atomic weight, low lipophilicity, and corruption by proteolytic enzyme and proteinase discharged within the bum [2]. Nanoparticles are accounted that increment the take-up of medication through varied system which includes transcellular retention, paracellular transport by gap tight intersection, Pgp hindrance, restraint of gut divider digestion by CYP450, and upgrade of humour vehicle [3]. Nanoparticles of size one hundred nm are viewed as ideal for humour transport of lipoid nanoparticle [4].

This aim of this review is to explain the challenges connected with the utilization of typical formulations against cardiovascular disease and advantage of oral nanoparticle drug delivery system within the treatment of high BP. This text addresses additional advanced technique or technology for increasing the efficaciousness medication of medicine employed in as medicine drugs. Majority of the medicine are coming back from category two BCS means that low solubility and high porousness, therefore their bioavailability is low as a result of dissolution rate is limiting. Each medicine was delivered by utilizing nanoemulsion as a drug delivery system. Chronotherapeutics; in nanosize in vary can extra be easier and economical upset and has been mentioned in liquid emulsion. Factor silencing is that recent technology where the use of little officious ribonucleic acid is finished to silence those receptors that concerned at intervals the rise of force per unit space IV route of

administer is most ordinarily used route for delivery of silencing ribonucleic acid. Varied experiments has been for oral delivery of silencing ribonucleic acid for cardiovascular disease has been formulate microencapsulated nanogel for the aim of oral delivery of silencing ribonucleic acid and checked their activity against inflammatory gut unwellness by targeting TNF-a [5].

LITERATURE REVIEW

Conventional drug therapy as an antihypertensive agent

The first antihypertensive drug pentaquine which was developed in 1960. On analysis it had been creation that this drug has several facet impacts with terribly low pharmacologic impact. After that in 1950 second antihypertensive ganglionic blocking agent was developed that conjointly also showed some disadvantages. Similarly many antihypertensive drugs like veratrum, hydralazine reserpine, diuretics and b-blockers also showed some adverse reaction. In 1990s, first-line antihypertensive drug was introduced. Classification of first-line antihypertensive drug are calcium channel blockers, di-hydropyridine calcium channel blockers, thiazide ,diuretics angiotensin and angiotensin converting enzyme inhibitors, loop diuretics, b-Adrenergic blocking agents, mineralocorticoid receptor blockers, centrally acting a-agonists etc. This initial first line drugs are most commonly prescribed drug in present days in single form or in combination form also.

There is striking progress in the exploitation of new therapeutics, which directly target Renin Angiotensinogen Aldosterone System (RAAS). Some novel objectives which have been developed for new possibility for the development of the antihypertensive drug for treating hypertension. This line medicine area unit most typically prescribed drug in gift days in single type or together type conjointly. There's dramatic progress within the development of novel medical specialty, the target of that is additionally connected to of proteinase angiotensinogen mineralocorticoid system RAAS. Some novel objectives that are developed for brand spanking new chance for the event of the medicament for treating cardiovascular disease, that area unit presently below presymptomatic and clinical stages of development area unit demonstration in Figure 1.

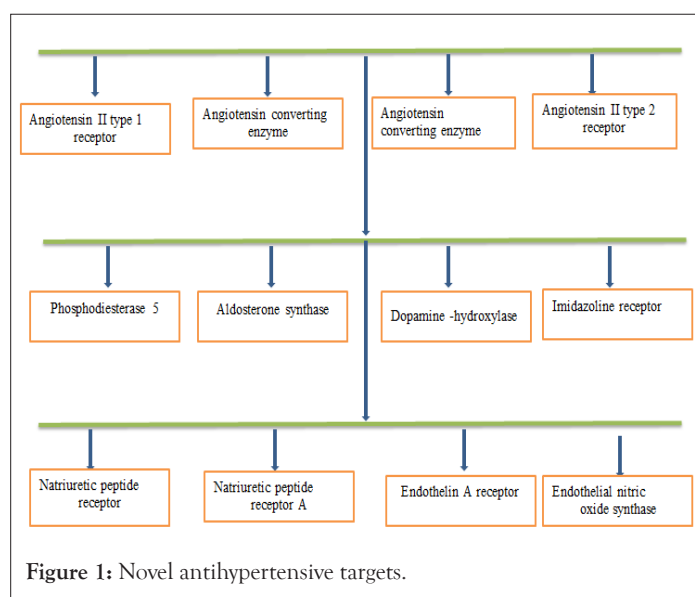**Figure 1:** Novel antihypertensive targets.

Angiotensin Ii type receptor agonist: Angiotensin type II receptor has action opposite to that of angiotensin type I receptor. It also shows opposite against the Angiotensin I-mediated vasoconstrictor

action of angiotensin along with this type II. Angiotensin II type receptor also shows vasodilatory action which is shaped of cGMP, bradykinin and nitric oxide.

Angiotensin Converting Enzyme (ACE): Angiotensin Converting Enzyme 2 (ACE2) induces metabolism of angiotensin receptor both I and II. This both angiotensin receptor both I and II which are the key peptides for Renin Angiotensinogen Aldosterone System (RAAS).

Aldosterone synthase inhibitor: For the biosynthesis of aldosterone, Aldosterone synthase is involved which is a cytochrome P450 enzyme and Inhibitor of this aldosterone synthase induced in disruption of Renin Angiotensinogen Aldosterone System (RAAS). This increases the blood pressure. Endothelin a receptor antagonist: Endothelin adheres with endothelin receptor and it carried on cell membrane and develops effects like systemic and pulmonary vasoconstriction apart from fibrinogenesis, atherosclerosis, oxidative damage, salt and water retention. Several antihypertensive drugs admitting new antihypertensive along with their mechanism of action and Pharmacological classification are reported in Table 1.

DISCUSSION

Limitation with oral delivery of antihypertensive

Oral delivery is the most commonly used route of administration of drug. Oral delivery has several advantages as compared to other routes. Still several compounds are unsuccessful in research and development due to their low bioavailability upon oral administration [6]. The low bioavailability is not able to reach the minimal effective attention to showcase healing movement [7,8]. A number of the motives for negative bioavailability are as follows: a)one of the motives is poor solubility of drugs that impacts the bioavailability as drug ought to be found in solution shape at absorption web page; b)some other is inappropriate partition coefficient as it influences the permeation of drug through lipid membrane; c)first-skip metabolism causes metabolism of drug which ends up in bad absorption and coffee bioavailability of the drugs; d)P-glycoprotein mediated efflux also changed into shown to modify the pharmacokinetics of drug; the presence of P-glycoprotein in the liver, kidney, and intestine causes discount in absorption of drug from the gastrointestinal tract and growth in drug removal; an antihypertensive drug, talinolol, is a Pgp substrate whose oral bioavailability is restrained by using P-glycoprotein mediated efflux; and e)degradation of drug within the gastrointestinal tract because of pH of the belly or enzymatic degradation or by means of chemical reactions also alters oral bioavailability of drugs [9]. Some reasons for poor oral bioavailability of poorly water soluble drugs are demonstrated below in Figure 2.

The solubility of drug is a challenging question in the therapeutic efficacy especially for the drugs with high aqueous solubility and epithelial permeability. According to the Biopharmaceutical Classification (BCS) drugs are characterized like a) BCS class I (↑solubility and ↑permeability) b) BCS class II (↓ solubility and ↑permeability) c) BCS class III (↑solubility and ↓ permeability) d) BCS class IV (↓ solubility and ↓ permeability). The oral bioavailability of some drugs is struck by their poor GI permeability. To reach the effective therapeutic activity, these drugs have to be prescribed at a high dose [10].

Commonly the solubility and permeability are most dependent factor for the oral absorption any drug. Most of the antihypertensive drug like nicardipine, deltiazem, and nifedipine are the prospect for the P-glycoprotein-intermediated efflux transporter which is present in the wall of intestinal but it is apart from cytochrome P450-intermediated enzymatic metabolism likewise the drugs which are under Biological Classification System (BCS) class 2 also show different pattern of absorption and bioavailability [11]. So the antihypertensive drug which are comes under this BCS class 2 also represents the different drug metabolism, different permeability, different solubility etc., more or less of which are discussed in Table 2. The above table symbolized that metabolism and solubility is the most important parameters because which determine the bioavailability as well as therapeutic effectiveness of the antihypertensive drug.

Table 1: Novel antihypertensive drug with their mechanism of action and pharmacological classification.

Sr.No	Antihypertensive drug class	Name of drug	Mechanism of action
1.	Angiotensin-converting enzyme inhibitors	Captopril, Enalapril, Lisinopril, Perindopril, Ramipril, Benazepril, Trandolapril, Fosinopril, Imidapril	Angiotensin-Converting Enzyme Inhibitors (CEis) block the conversion of angiotensin I to the II potent vasoconstrictor peptide angiotensin II.
2.	Angiotensin receptor blockers	Losartan, Valsartan, Telmisartan, Candesartan, Irbesartan,Olmesartan, medoxomil	Angiotensin Receptor Blockers (ARBs) competitively block the angiotensin II receptors.
3.	Dihydropyridine calcium channel blockers	Verapamil, Diltiazem, Nifedipine, Felodipine, Amlodipine, Nitrendipine, Lacidipine, Benidipine, Lercanidipine	Calcium channel blockers bind to the a1-subunit of the L-type calcium channel in muscle cell membranes, reducing calcium flux through the channels and lowering cytosolic calcium concentration, which ultimately reduces muscle contractility.
4.	Thiazide diuretics	Hydrochlorothiazide,Chlorthalidone,Indapamide	Thiazides inhibit the Nacl transporter in the distal convoluted tubule of the nephron, which is responsible for around 5% of total sodium reabsorption.
5.	Loop diuretics	Furosemide	Inhibit the Na-K-2Cl transporter in the apical membrane of kidney tubular epithelial cells located in the thick ascending limb of the loop of Hence, which is responsible for around 25% of sodium reabsorption under normal conditions.

| 6. | b-Adrenergic blocking agents | Propranolol, Metoprolol Atenolol, Bisoprolol 2Nebivolol Oxprenolo | It blocks the b1-adrenergic receptors which reduced heart rate and cardiac contractility. |
7.	Mineralocorticoid receptor blockers	-	Mineralocorticoid Receptor Blockers (MRBs) competitively inhibit aldosterone binding to the mineralocorticoid receptor, which ultimately increases epithelial sodium channel degradation and thus, results in reduced sodium reabsorption at the expense of reduced potassium excretion.
8.	Director vasodilators	Hydralazine Minoxidil Diazoxide	Hydralazine reduces intracellular calcium in vascular smooth muscle cell.
9.	Centrally acting a-agonists	Clonidine,Methyldopa	Stimulate a2-receptors in the brainstem, reducing sympathetic outflow.

Figure 2: Causes for poor oral bioavailability of poorly water soluble drugs.
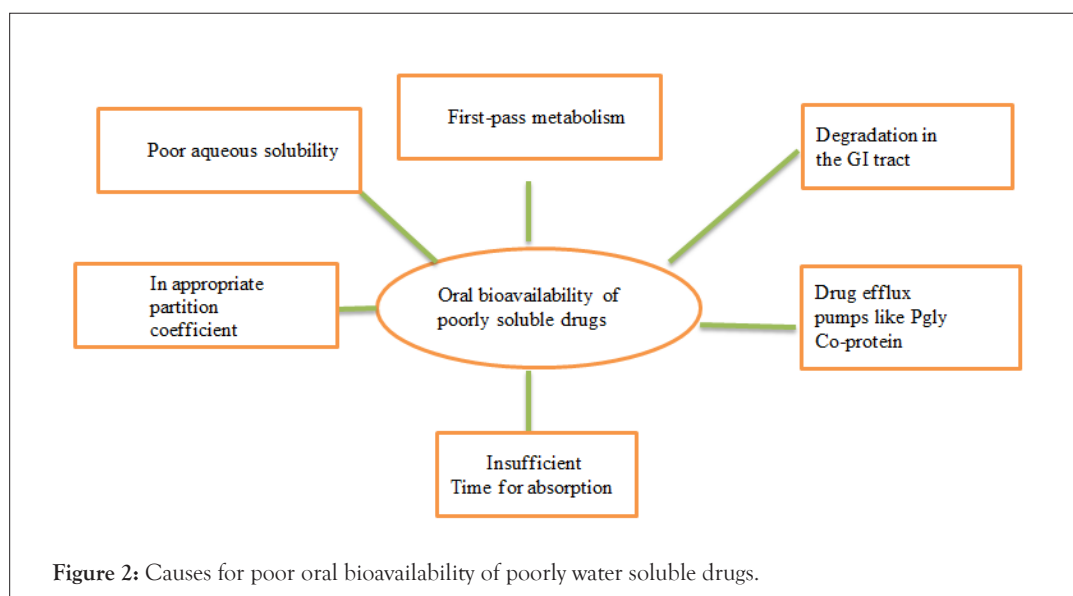
Table 2: Metabolism, permeability & solubility of some antihypertensive drug.

Class	Drug	Metabolism	Solubility
Calcium channel blocker	Felodipine	Inclusively metabolized by CYP3A4	7.15 mg/ml
	Amlodipine	Metabolized by CYP3A4	75.3 mg/ml
	Nifedipine	Hepatic metabolism by CYP3A	20 mg/ml
	Verapamil	Extensively metabolized by CYP2C8, CYP2C18, and CYP2C9	7 mg/ml
	Nisoldipine	Extensive gut wall metabolism, CYP3A4 substrate	5.7 mg/ml
Angiotensin receptor blockers	Olmesartan	Not metabolized by cytochrome P450 but is metabolized by liver esterase	7.75 mg/ml
Beta blocker	Carvedilol	CYP1A2, CYP3A4, CYP1A1 CYP2D6, CYP2E1, CYP2C9	0.583 mg/ml

Nanotechnology in delivery of poorly soluble drugs

Drugs with poor solubility have displayed difficulty in formulations that is poor oral bioavailability , reduce onset of action, failure in order to get regular assert plasma concentration, undesirable side effects and lack of dose proportionality and unpleasant patient compliance These challenges of customary dosage forms can be defeat by using Novel Drug Delivery Systems (NDDS) that supply profits like, lowering of dose size, reduction in dose frequency, enhanced permeability, improvement in oral bioavailability and web page particular targeting [12–16]. Nanotechnology is a predicting approach in the development of oral drug delivery. Systems specially inadequate bioavailability, poor biopharmaceutical properties unpleasant solubility and low permeability, The vast majority of current nanotechnology utilized in development of oral drug delivery systems are micelles, polymeric nanoparticles, solid lipid nanoparticles, nanoemulsions, liposomes, etc. which supply sustained, controlled and targeted drug delivery. Nanoparticle seems to be the higher advance to get rid of the not enough associated with oral delivery of medicament. Diverse nanoparticulate systems love chemical compound nanoparticle, green nanoparticle, and lipid based nanoparticle love nanocapsule, nanoemulsion, SLN, NLC etc. are studied to overcome the limitation of oral delivery of drug. Polymeric nanoparticle supplies the benefit of protective PH sensitive antihypertensive drug love nisoldipine. Chitosan based nanoparticle degrades at the enteral PH. Likewise magnetic nanoparticle is repeatedly targeted to an area regardless drug inharness is wanted thoroughly outwardly applied field [17]. The utilization of nanotechnology in drug delivery entity have extensively been looked into improvement of the bioavailability of antihypertensive drugs [18,19]. Several of the investigations on utilization of nanotechnology on antihypertensive drugs are served in Table 3.

Table 3: Some of the investigations on utilization of nanotechnology on antihypertensive drugs.

Antihypertensive drug	Nanotechnology	Application
Felodipine	Nanosuspensions	Enhanced solubility and oral bioavailability
	Polymeric nanoparticles	Controllable drug release and effective *in vitro* compatibility
Carvedilol	Nanosuspensions	Increased oral bioavailability
	Solid lipid nanoparticles	Enhanced bioavailability and protecting it from acidic environment
	Carbon nanotubes	Drug loading capacity and improving the solubility
Valsartan	Polymeric nanoparticles	Prolonged release of drug and thereby it decreases its dose size, frequency of dose, and side effects
	Nanosuspensions	Enhanced drug release
	Self-nanoemulsifying drug delivery system	Increase in dissolution rate
	Solid lipid nanoparticles	Bypassing first-pass metabolism, enhancing lymphatic absorption, and improving solubility and bioavailability
Nebivolol	l Polymeric nanoparticles	Prolonged drug release
Nifedipine	Polymeric nanoparticles	Improved oral bioavailability
	Dendrimers]	Enhanced water solubility
	Nanocrystals	Enhanced dissolution rate
Nitrendipine	Nanocrystals	Improvement in physical stability, *in vitro* drug release, and bioavailability
Candesartan cilexetil	Dendrimers	Improved water solubility
	Nanosuspension	Improved bioavailability
	Polymeric micelles	Micelles Increased drug loading capacity and drug release

Several other antihypertensive drugs like valsartan, medoxomil, olmesartan lacidipine, and carvedilol prove the poor bioavailability due to enzymatic degradation and low aqueous solubility. But when these drugs are presented in the form of nanoemulsion for drug delivery it shows determined response [20]. Likewise other type of nanoparticles for example Solid lipid nanoparticles was additionally developed to double the bioavailability of several antihypertensive drug love isradipine, Candesartan and nisoldipine. Solid Lipid Nanoparticles (SLN) comprises of solid lipid particle which is surrounded by surfactants and this SLN has benefits that they're presented in both liquid emulsion and polymeric nanoparticle form. SLN are composed up from biocompatible biological lipids, so they're biodegradable in bio fluid [21].

Novel nanocarriers for the antihypertensive drug delivery

Polymeric nanoparticles: Polymer loaded nanoparticles or polymeric nanoparticles are the vast majority of extensively looked for oral antihypertensive drug delivery. This polymer based nanoparticles alive to hydroxy propyl methyl cellulose, poly-e caprolactone, polylactide-coglycolide, chitosan, Eudragit etc. rolling out of drug from polymer loaded nanoparticles is largely positive by the particle size, technique of preparation, molecular weight of polymer, surfactants, and polymer architecture etc. pH sensitive antihypertensive drugs love require to be given in intestine only in these case PH-sensitive polymers is Utilized which can give the drug at particular web page of GIT. Likewise drugs which are destroyed in acidic medium, copolymer are utilized to given in the colon as those drugs are generous to degradation at GIT. Utilized of these polymeric nanoparticle assists in tissue targeting delivery of drug, enhancing the drug solubility, delivery of bio therapeutics

[22]. Studied that the roll out of antihypertensive drug nisoldipine loaded Eudragit S100 nanoparticle and was found that the rolling out of drug count on pH of the colon. Therefore it was obvious that the formulation containing polymeric nanoparticle has the capability to double the bioavailability of the drug.

Chitosan nanoparticle: Chitosan is natural nontoxic, biocompatible and perishable carbohydrate this bio adhesive carbohydrate is wide used as site-specific and sustained release delivery of most of medication. Chitosan loaded nanoparticles have exaggerated the bioavailability of drug by keeping first-pass metabolism and additionally by preventing the degradation of drug at acidic pH scale [23].

Hydroxypropyl Methyl Cellulose (HPMC) nanoparticle: HPMC is a water-soluble cellulose derivative mainly used for manufacturing a dosage form which is to be required controlled release of drug. HPMC is available in different type by calculating the concentration of hydroxypropoxyl and methoxy group. antihypertensives drug loaded HPMC showing low bioavailability as compared to the unit solid tablet dosage form.

Lipid-based nanoparticles: Lipid-based nanoparticles for the delivery of antihypertensive drug establishing the low solubility and high permeability. Lipid based nanoparticles trapped drug which are poorly soluble. The process of solubilization of drug is normally maintained by the gastrointestinal passage. The additives used for preparing the Lipid based nanoparticles consist of surfactants and co surfactants. This can improve the permeability of drug through the intestinal wall. The fundamental mechanism of the increasing absorption of drug admit opening of tight junction, increase in membrane fluidity, alteration of intestinal metabolism mediated

by cytochrome P450, lymphatic uptake, and inhibition of P glycoprotein efflux transporter [24].

Liquid emulsion: Liquid Emulsion (LE), Self-Nanoemulsifying Drug Delivery System (SNEDDS), Self-Microemulsifying Drug Delivery System (SMEDDS), microemulsion, and nanoemulsion. SNEDDS and SMEDDS are the sort of nanoemulsion as a result of they create nanoemulsion at within the gastrointestinal milieu only. And so it is then taken up by lymphatic tract. These Liquid emulsion systems accommodate natural or artificial oil, co-surfactants and surfactants. These liquid emulsions are the mixtures of emulsifying agent with the excipients. SNEDDS and SMEDDS are a lot of stable as compared to the nanoemulsion as a result of they're in a roundabout way contact with binary compound medium.

Nanoemulsion drug delivery systems are thermodynamically stable. This nanoemulsion will solubilize a lot of or higher quantity of drug. This kind of Nano carriers may be used for targeted delivery of drug. According to researcher nanoemulsion accomplish most oral bioavailability.

Solid lipid nanoparticles: Solid Lipid Nanoparticles (SLNs) are prepared from the biocompatible solid lipid macromolecule excipients together with co-surfactants and wetting agent. Different excipients utilized in the preparation of SLNs SLNs are monoglycerides, diglycerides, and triglycerides of fatty acid Due to the combination of these glycerides in the SLNs it is not perfect crystal for the accumulation of drug into it. SLN embrace enriched shell, SLN matrix, compound Mixed and drug enriched core kind. Preparation of SLN chiefly depends on the character of solid macromolecule and drug used. The delivery of drug from SLN nanoparticle is followed biphasic rule as at the start it burst adopted by sustained unleash. Then burst unleash is controlled by lowering the temperature and concentration of wetting agent throughout producing. . SLNs increase the bioavailability of drug by rendering first-pass metabolism as they need direct bodily fluid uptake. Researchers have theorized that nanoparticle that binds to the GI membrane, gains the abidance time of SLN. The utilization of surfactants like phosphatidylcholine and poloxamer within the SLN increase the porosity of drug across the GI membrane.

Thus, nano drug delivery system plays a very important role in amending the therapeutic edges of the many artificial also as flavourer medicine whether or not. Engineering improved the drug performance through either providing sustained unharness or preventing their degradation.

CONCLUSION

Nanotechnology applies an excellent potential in edges in drug delivery especially poorly soluble medicament medication by rising oral bioavailability and solubility. New coeval's antihypertensive drugs, novel molecular targeting drug delivery and Nano carrier based drug delivery system are presently in polar level of clinical trial and the results showing a very good positive result. Lots of new molecular targeting delivery for antihypertensive are still under exploratory phase and are equalling challenged with already-established antihypertensive drug therapy as follows their effectiveness is also concerned but there is even some assess of improvement in the drug therapy. Nanocarriers or using of s nanotechnology is anticipating advanced in resolving the several restraints of antihypertensive drug delivery Targeted drug delivery through the nanocarriers will effectively take medicament medical

care and its website of action whether or not it's heart, excretory organ or sleek muscle. Cistron targeting technology is additionally another fashionable therapeutic tool that is additionally playing a very important role in succeeding within the treatment of high blood pressure. Gene targeting technology is also another modern therapeutic tool which is also play an important role in succeeding in the treatment of hypertension. Various challenging question in the gene delivery like pharmacokinetics, pharmacodynamics, cellular uptake etc. could be defeat by the using suitable nanocarriers. Finally the outcomes of the treatment mainly depends upon the skillfullness of the nanotechnology which can frame a wide form of molecule like proteins and peptides and also its targeting site from its stability in the physiological condition as well as in the external environment also.

CONFLICT OF INTEREST

The authors confirm that they have no conflicts of interest with respect to the work described in this manuscript.

REFERENCES

1. Pan WH, Chang HY, Yeh WT, Hsiao SY, Hung YT. Prevalence, awareness, treatment and control of hypertension in Taiwan: results of Nutrition and Health Survey in Taiwan (NAHSIT) 1993–1996. J Hum Hypertens. 2001;15(11):793-798.

2. Pridgen EM, Alexis F, Farokhzad OC. Polymeric nanoparticle technologies for oral drug delivery. Clin Gastroenterol Hepatol. 2014;12(10):1605-1610.

3. Nanjwade BK, Patel DJ, Udhani RA, Manvi FV. Functions of lipids for enhancement of oral bioavailability of poorly water-soluble drugs. Sci Pharm. 2011;79(4):705-728.

4. Ghosh S, Roy T. Nanoparticulate drug-delivery systems: lymphatic uptake and its gastrointestinal applications. J Appl Pharm Sci. 2014;4(6):123-130.

5. Knipe JM, Strong LE, Peppas NA. Enzyme-and pH-responsive microencapsulated nanogels for oral delivery of siRNA to induce TNF-α knockdown in the intestine. Biomacromolecules. 2016;17(3):788-797.

6. Agrawal U, Sharma R, Gupta M, Vyas SP. Is nanotechnology a boon for oral drug delivery? Drug Discov Today. 2014;19(10):1530-1546.

7. Li H, Zhao X, Ma Y, Zhai G, Li L, Lou H. Enhancement of gastrointestinal absorption of quercetin by solid lipid nanoparticles. J Control Release. 2009;133(3):238-244.

8. Khadka P, Ro J, Kim H, Kim I, Kim JT, Kim H, et al. Pharmaceutical particle technologies: An approach to improve drug solubility, dissolution and bioavailability. Asian J Pharm Sci. 2014;9(6):304-316.

9. Tambosi G, Coelho PF, Luciano S, Lenschow IC, Zétola M, Stulzer HK, et al. Challenges to improve the biopharmaceutical properties of poorly water-soluble drugs and the application of the solid dispersion technology. Matéria (Rio de Janeiro). 2018;23.

10. Gupta H, Bhandari D, Sharma A. Recent trends in oral drug delivery: a review. Recent Pat Drug Deliv Formul. 2009;3(2):162-173.

11. Zisaki A, Miskovic L, Hatzimanikatis V. Antihypertensive drugs metabolism: an update to pharmacokinetic profiles and computational approaches. Curr Pharm Des. 2015;21(6):806-822.

12. Jain N, Jain R, Thakur N, Gupta BP, Jain DK, Banveer J, et al. Nanotechnology: a safe and effective drug delivery system. Asian J Pharm Clin Res. 2010;3(3):159-165.

13. Singh R, Lillard Jr JW. Nanoparticle-based targeted drug delivery. Exp Mol Pathol. 2009;86(3):215-223.

14. Safari J, Zarnegar Z. Advanced drug delivery systems: Nanotechnology of health design A review. J Saudi Chem Soc. 2014;18(2):85-99.

15. Kalepu S, Nekkanti V. Insoluble drug delivery strategies: Review of recent advances and business prospects. Acta Pharm Sin B. 2015;5(5):442-453.

16. Kaparissides C, Alexandridou S, Kotti K, Chaitidou S. Recent advances in novel drug delivery systems. J Nanotechnol. 2006;2:1-1.

17. Antal I, Kubovcikova M, Zavisova V, Koneracka M, Pechanova O, Barta A, et al. Magnetic poly (d, l-lactide) nanoparticles loaded with aliskiren: A promising tool for hypertension treatment. J Magn Magn Mater. 2015;380:280-284.

18. Mei L, Zhang Z, Zhao L, Huang L, Yang XL, Tang J, et al. Pharmaceutical nanotechnology for oral delivery of anticancer drugs. Adv Drug Deliv Rev. 2013;65(6):880-890.

19. Dwivedi DK, Singh AK. Dendrimers: A novel carrier system for drug delivery. J Drug Deliv Ther. 2014;4(5):1-6.

20. Sharma N, Bansal M, Visht S, Sharma PK, Kulkarni GT. Nanoemulsion: A new concept of delivery system. Chronicles of Young Scientists. 2010;1(2):2-6.

21. Shah U, Joshi G, Sawant K. Improvement in antihypertensive and antianginal effects of felodipine by enhanced absorption from PLGA nanoparticles optimized by factorial design. Mater Sci Eng C. 2014;35:153-163.

22. Koziolek M, Grimm M, Becker D, Iordanov V, Zou H, Shimizu J, et al. Investigation of pH and temperature profiles in the GI tract of fasted human subjects using the Intellicap® system. J Pharm Sci. 2015;104(9):2855-2863.

23. Niaz T, Shabbir S, Manzoor S, Rehman A, Rahman A, Nasir H, et al. Antihypertensive nano-ceuticales based on chitosan biopolymer: Physico-chemical evaluation and release kinetics. Carbohydr Polym. 2016;142:268-274.

24. Neves AR, Queiroz JF, Lima SA, Figueiredo F, Fernandes R, Reis S. Cellular uptake and transcytosis of lipid-based nanoparticles across the intestinal barrier: Relevance for oral drug delivery. J Colloid Interface Sci. 2016;463:258-265.