Hyperlipidemia is an elevated condition of lipid levels in the body and is known to speed up a process of atherosclerosis that may prove fatal in the development of various cardiovascular diseases. Increase in lipids like LDL i.e low density lipoproteins, cholesterol and triglycerides are mainly responsible for hyperlipidemia. Present pharmacotherapy for hyperlipidemia includes statins, niacin, fibric acid derivatives and cholesterol absorption inhibitors. 90% of the pharmacotherapy of hyperlipidemia includes statins and these statins also suffer from limitations like, inadequate solubility, less absorption, less bioavailability and ineffectiveness in lowering of cholesterol levels only up to maximum 40% risk reduction. These drugs are to be given on daily basis which make it cumbersome for patients. Novel Drug Delivery System is an advanced drug delivery system with improved solubility, absorption, bioavailability, drug potency, control drug release to give a sustained therapeutic effect, and target oriented to a desired tissue as well as patient compliance is good. So it is the need of hour to formulate such kind of drug delivery systems which will combat the limitations of antihyperlipidemic therapy. The present review emphasise on applications of novel drug delivery systems in pharmacotherapy of anti hyperlipidemic drugs.

**KEY WORDS:** Hyperlipidemia, Pharmacotherapy, Novel drug delivery system, Bioavailability.

**INTRODUCTION**

Hyperlipidemia is a condition in which there are abnormally high levels of lipids i.e. the fatty substances which are found in the blood. This condition is also known as hypercholesterolemia or hyperlipoproteinemia [Table 1]. Increase in lipids like LDL i.e. low density lipoproteins, cholesterol and triglycerides are mainly responsible (Gupta, 2011). Hyperlipidemia occurs when the diet contains too much cholesterol and fat or when body produces too much cholesterol and fat or both. Primary reason for hyperlipidemia is the defect in lipid metabolism which is due the lipoprotein lipase activity or the absence of the surface Apo protein C-II (Gupta, 2011; Rohilla, 2012). There are various other causes like genetic abnormalities and environmental factors (Toth, 2001). Hyperlipidemia is the major cause of atherosclerosis and other conditions related to atherosclerosis like coronary heart disease, peripheral vascular disease, ischaemic cerebrovascular disease and pancreatitis (Gupta, 2011). It has been proved that elevated plasma levels of cholesterol and LDL are the main reasons of atherosclerosis whereas, plasma levels of HDL have a protective effect (Bhatnagar, 2008). Complications from high cholesterol and triglycerides affect the heart. These complications include heart disease, heart attack, and stroke (Kahn, 2012).

According to World Health Organisation, 2002 almost 18% of the total stroke events and about 56% of heart disease in world are due to total cholesterol levels above 3.2 mmol /L. This accounts for a total of 4.4 million deaths i.e. 7.9% and 2.8% of the global disease burden (Talbert, 1999). 55% of population has an increased plasma lipid level resulting in increased risk of CHD. Almost 2000 in 100000 people have plasma cholesterol more than 292 mg/dL. Familial combined hyperlipidemia is found in 500 out of 100000 and familial dysbetalipoproteinemia is only in 1% of the total population (Gauer, 2010).

| Table 1: Total cholesterol levels in adults(Dog, 2003; Mallya, 2012; Kahn, 2012.) |
|-----------------|-------------------|-------------------|-------------------|
| **Cholesterol** | **Normal level**  | **Borderline level** | **High level**   |
| 150-200 mg/dL   | 200-239 mg/dL     | Above 250 mg/dL    |
| 160-200 mg/dL   | 200-239 mg/dL     | Above 250 mg/dL    |
| 189 mg/dL       | 200-239 mg/dL     | Above 250 mg/dL    |
| **Triglycerides** | **Normal level**  | **Borderline level** | **High level**   |
| 5-32 mg/dL      | 32-40 mg/dL       | Above 40 mg/dL     |
| **HDL**         | **Normal level**  | **Borderline level** | **High level**   |
| 40-60 mg/dL     | 60-60 mg/dL       | Below 40 mg/dL     |
| 130-159 mg/dL   | 160-189 mg/dL     | Below 40 mg/dL     |
| **LDL**         | **Normal level**  | **Borderline level** | **High level**   |
| 100 mg/dL       | 130-159 mg/dL     | 160-189 mg/dL      |
| **VLDL**        | **Normal level**  | **Borderline level** | **High level**   |
| 5-32 mg/dL      | 32-40 mg/dL       | Above 40 mg/dL     |

Pathophysiology of hyperlipidemia: Fats are insoluble in water and combine with another substance called a protein to create a lipoprotein. These lipids are associated with blood and remain dissolved in it. There are three kinds of lipoproteins in our body (Dog and Ritley, 2003; Jehle, 2002)

- Low density lipoprotein or LDL
- High density lipoprotein or HDL
- Very low density lipoprotein or VLDL

Cholesterol is made up of these three lipoproteins. Low density lipoproteins in excessive quantities accelerate the deposition of LDL on artery walls and lead to atherosclerosis while as the high density lipoproteins prevent the deposition of LDL on artery walls and hence are preventive in nature (Jehle, 2002). Arteries are normally smooth and unobstructed on the inside but when there is increase in lipid level, a sticky substance called plaque is formed inside the walls of arteries (Mandal, 2013). This leads to reduced blood flow, which leads to...
stiffening and narrowing of the arteries (Libby, 2011). Pathophysiology of hyperlipidemia can be categorized into primary and secondary hyperlipidaemia (Yuan, 2007). Primary hyperlipidemia involves the idiopathic hyperchylomicronemia defect in the lipid metabolism caused by a defect in lipoprotein lipase activity or due to absence of surface apoprotein C II. Primary hyperlipidemia can occur either due to over production or impaired removal of lipoproteins while as the secondary one is either due to the defect in lipoprotein or its receptor.

Primary hyperlipidemia is inherent in person that is it has genetic effect while as the secondary is due to other disease like diabetes mellitus, hypothyroidism, chronic renal failure, obesity, alcohol, etc. (Grundy, 1984). These factors worsen the condition of the person having primary hyperlipidemia. Primary hyperlipidaemia is due to single gene defect it is familial and called as monogenic or genetic and poly gene defect which is a multiple genetic defect (Gupta, 2011). Primary hyperlipidemia can be further categorised in to different (i) Type I familial hyperchylomicronemia, (ii) Type II familial hypercholesterolemia, (iii) Type IIB familial combined(mixed) hyperlipidemia, (iv) Type III familial dysbetalipoproteinemia, (v) Type IV familial hypertriglyceridemia, (vi) Type V familial mixed hypertriglyceridemia (Grundy, 1984).

In case of liver disease hypercholesteremia has been noted to be caused by reduced excretion of cholesterol in bile and in that of a nephrotic syndrome the common synthetic pathway for albumin and cholesterol causes low oncotic pressure which then leads to enhanced cholesterol synthesis (Dipiro, 2008).

Secondary is associated with other diseases like diabetes, myxoedema, chronic alcoholism, with use of drugs like corticosteroids, oral contraceptives and beta –blockers (Gupta, 2011). There are four types of secondary hyperlipidaemia (Gupta, 2011):- (i) Hypercholesterolemia, (ii) Hypertriglyceridemia, (iii) Hypocholesterolemia and (iv) Low HDL.

Present therapy: Initial therapy for any lipoprotein disorder is dietary restriction of total saturated fat and cholesterol and an increase in polyunsaturated fat intake along with regular exercise (Talbert, 1999; Havel, 1995). The objectives of dietary therapy are to decrease the intake of total fat, saturated fatty acids (i.e., saturated fat), and cholesterol progressively and to achieve a desirable body weight (Gupta, 2011). Several different classes of drugs are used to treat hyperlipidemia. These classes differ not only in their mechanism of action but also in the type of lipid reduction and the magnitude of the reduction. Statins, the most common group of anti-hyperlipidemic drugs lowers cholesterol by interrupting the cholesterol biosynthetic pathway. On the other hand, fibrate group decrease fatty acid and triglyceride levels by stimulating the peroxisomal b-oxidation pathway (Jain, 2007).

There are three most commonly used combination therapies for hyperlipidemia:–
1. Statin and Ezetimibe combination therapy. (Dufaux, 1982; Last, 2011).
2. Statin and fibrate combination therapy. (Papadakis, 1999; Spence, 1995).
3. Ezetimibe and fibrate combination therapy. (Craig, 2010).

Conventional drug delivery system: Perspective drug delivery systems can be defined as mechanisms to introduce therapeutic agents into the body. Those methods included pills, syrups, capsules, tablets, elixirs, solutions, extracts, emulsions, suspension, cachets, troches, lozenges, nebulizers, and many other traditional delivery mechanisms. Most common routes of administration include the preferred non-invasive peroral (through the mouth), topical (skin), transmucosal (nasal, buccal/ sublingual, vaginal, ocular and rectal) and inhalation routes (Talele, 2013). The various limitations of Conventional Drug Delivery Systems are:– Unfavourable biodistribution, low bioavailability, lack of water solubility, poor delivery to the intended site of action, low therapeutic response despite high dosages, side effects, drug resistance, toxicity, barriers in the body such as the blood brain barrier. All these limitations lead to the development of novel drug delivery systems (Sharma and Singh, 2011).

Novel drug delivery systems: Novel Drug Delivery System is an advance drug delivery system which improves drug potency, control drug release to give a sustained therapeutic effect, improve pharmacological utilities of drugs, provide greater safety; finally it is to target a drug specifically to a desired tissue. The drug should be administered to fulfil three criteria, including successful release of the drug in the targeted body part, in addition to the initial encapsulation. The usefulness of drug delivery systems is based on the ability to manipulate the biodistribution and pharmacokinetics (Choudary, 2012). Conventional forms of drug administration generally rely on pills, eye drops, ointments, and intravenous solutions. Recently, a number of novel drug delivery approaches have been developed. These approaches include drug modification by chemical means, drug entrapment in small vesicles that are injected into the bloodstream, and drug entrapment within pumps or polymeric materials that are placed in desired bodily compartments (for example, the eye or beneath the skin) (Langer, 1990; Farrokhi, 2012). Various drug delivery and drug targeting systems are currently under development to minimize drug degradation and loss, to prevent harmful side-effects and to increase drug bioavailability and the fraction of the drug accumulated in the required zone (Reddy, 2010). Among drug carriers one can name soluble polymers, microparticles made of insoluble or biodegradable natural and synthetic polymers, microcapsules, cells, cell ghosts, lipoproteins, liposomes and micelles. The carriers can be made slowly degradable, stimuli-reactive (e.g.
Fewer side effects and adverse reactions, has low oral bioavailability due to its solubility and dissolution limitations. Numerous advantages of novel drug delivery systems are:

- Improved solubility and bioavailability
- Improved pharmacokinetics
- Sustained release profiles for longer times
- Increasing the gastrointestinal absorption through passive diffusion

SMEDDS

An optimized SMEDDS forLovastatin is poorly soluble in gastric fluid when administered through conventional dosage forms like tablet, so by increasing gastrointestinal absorption through passive diffusion the mixtures of oil, water and surfactants sometimes they may require co.

Different Novel Drug Delivery Systems:

- Oral Delivery Drug Delivery Systems.
- Parenteral and Implant Drug Delivery Systems.
- Pulmonary and Nasal Drug Delivery.
- Transmucosal Drug Delivery.
- Transdermal and Topical Drug.

**NOVEL DRUG DELIVERY SYSTEMS FOR ANTI- HYPERLIPIDEMIC DRUGS**

Most of the anti hyperlipidemic drugs have poor water solubility hence poor dissolution which lead to poor bioavailability. So when these drugs are given in conventional dosage forms they do not meet the therapeutic requirements hence are given in large doses which lead to various side effects. Therefore it is the required to formulate that kind of dosage form in which the drug shows greater bioavailability and less side effects. Researches are going on in this field and various novel drug delivery systems are formulated and evaluated which have shown the increase in bioavailability of these drugs. Some of the novel drug delivery systems for anti hyperlipimic drugs are:

**Self-Micro Emulsifying Drug Delivery System:** Self-microemulsifying drug delivery systems (SMEDDS) are class of emulsion formulated to enhance the oral bioavailability of the poorly absorbed drugs. These systems are the mixtures of oil, water and surfactants sometimes they may require co-surfactants. The droplet size of these emulsions is less than 50 nm. Self-emulsifying formulations spread readily in the GI tract, and the digestive motility of the stomach and the intestine provide the agitation necessary for self-emulsification (Agrawal, 2012). Lovastatin is poorly soluble in gastric fluid when administered through conventional dosage forms like tablet, so SMEDDS are formulated to increase the solubility of drug in gastric fluid and hence improving the bioavailability by increasing gastrointestinal absorption through passive diffusion (Patela, 2010). Fenofibrate is a (BCS) Class II drug with a high dose number. Thus, has low oral bioavailability due to its solubility and dissolution limitations. An optimized SMEDDS formulation consisting of Labrafac CM10 (31.5% wt/wt), Tween 80 (47.3% wt/wt), PEG 400(12.7% wt/wt), and fenofibrate (8.5% wt/wt) has been developed with an increased dissolution rate, increased

<table>
<thead>
<tr>
<th>Drug class</th>
<th>Examples</th>
<th>Mechanism of action</th>
<th>Effect on lipids</th>
<th>Side effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydroxyl methyl glutarate coenzyme - A reductase inhibitor (Statins)</td>
<td>Lovastatin(10-80mg), Pitavastatin(1-4mg), Simvastatin(5-40mg), Pravastatin(40-80mg), Fluvastatin(20-80mg), Atorvastatin(10-80mg), Rosuvastatin(5-20mg), Pravachol(10-80mg).</td>
<td>Inhibits cholesterol synthesis by inhibiting the rate limiting HMG CoA reductase</td>
<td>LDL↓, HDL↑, TG↓</td>
<td>Myopathy, Rhabdomyolysis, Kidney failure, Cardiomyopathy, muscle tenderness, rise in serum transaminase</td>
</tr>
<tr>
<td>Bile acid sequestrants (Henley, 2002; Talbert, 1999; Moon 2007; Last, 2011)</td>
<td>Cholestyramine (4-16mg), Cholestipol (5-30mg), Colesevelam (3750mg).</td>
<td>Increase conversion of cholesterol into bile acids in hepatocytes, increase LDL receptors in hepatocytes, decrease bile acid absorption.</td>
<td>LDL↓, HDL↑</td>
<td>Constipation, Osteoporosis, Deficiency of Vit. A, D, E, &amp;K cause Flatulence, Interference with other drugs</td>
</tr>
<tr>
<td>Fibrates or lipoprotein lipase stimulants (Halpern, 1995; Obata, 2006; Papadakis, 1999).</td>
<td>Clofibrate (500mg), Gemfibrozil (1200mg), Fenofibrate (200mg), Ciprofibrate (100mg), Bezafibrate (600mg).</td>
<td>Increase lipolysis by increasing activity of lipoprotein lipase, decrease release of fatty acids from adipose tissue.</td>
<td>LDL↓, HDL↑, TG↓</td>
<td>G.I discomfort, Aching muscles, Sensitivity to sunlight, Skin rashes, Gall stones, Abnormal heart rhythms, Impoieny</td>
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Solubility thus, increased bioavailability of a poorly water-soluble drug (Patel, 2007). Supersaturated drug delivery systems contain the drug in a high-energy or rapidly dissolving form, which allows the solution to contain drug concentrations above the solubility limit. SEDDS are thermodynamically unstable; however the drug can easily precipitate, returning the solution to its equilibrium state. Supersaturable SEDDS have an additional advantage over conventional SEDDS, that they contain a reduced amount of surfactant hence have reduced surfactant side effects. SEDDS are designed to generate a supersaturated solution when released into an aqueous medium. Supersaturation increases the thermodynamic activity of a drug above its solubility. The increased force drives the drug across the GI barrier (Lincoln, 2012).

**Ternary Solid Dispersions:** Solid dispersions have been widely used to enhance the solubility, dissolution rate, and bioavailability of poorly soluble drugs. There are different types of solid dispersion systems categorized according to the physical states of the drug and the carrier in the systems. It may be a molecular solid solution, a dispersion of amorphous or crystalline drug particles in an amorphous carrier matrix or a combination of a solution and dispersion of solids. Fenofibrate compound is practically insoluble in water and has high lipophilicity. Thus the dissolution rate of fenofibrate is expected to limit its absorption from the gastrointestinal tract. The solid dispersion of the fenofibrate prepared by spray drying technique using Poloxamer 188 as carrier and TPGS as surfactant showed maximum solubility enhancement of fenofibrate (Bhise, 2011). Solid dispersion along with an adsorption technique that employs a water-soluble adsorbent can be used to enhance the dissolution of Ezetimibe, which may result from the combined effect of hydrophilic carriers and increased surface area (Parmar, 2011). Many drugs can be given in such form which will enhance the effectiveness of the drug.

**Nanosuspension:** Nanosuspension is a submicron colloidal dispersion of drug particles that are produced by suitable methods and stabilized by surfactants (Chingunpituk and Walailak, 2007). A pharmaceutical nanosuspension can be defined as the nano-sized drug particle which is finely dispersed in an aqueous vehicle for either oral and topical use or parenteral and pulmonary administration. In general, the particle size in nanosuspension is always less than 1 μm (usually lies between 200nm to 600nm) (Malakar, 2012). The reduction of drug particles into the sub-micron range leads to a significant increase in the dissolution rate and therefore enhances bioavailability (Chingunpituk and Walailak, 2007). Nanosuspensions not only increase the surface area but also simultaneously increase the saturation solubility and the solution velocity by increasing the vapour pressure of the particles. Here the dissolution velocity gradually gets increased due to decrease in the diffusional distance on the surface of drug nanoparticles. The saturation solubility gets affected through in situ generation of energies during conversion of drug microcrystals to nanoparticles. Fenofibrate is a nanosuspension currently marketed in the name of Tricor (Malakar, 2012). Nanosuspensions utilize some techniques to minimize the particle size to the nano level which help to improve the solubility of the drug due to small particle size.

**Ion Exchange Resins:** Ion exchange resins are cross-linked, water insoluble, polymer-carrying, ionizable functional groups. They contain acidic or basic functional groups and have the ability to exchange counter-ions within aqueous solutions surrounding them. An ion exchange resin is exhibited like small bead with a diameter between 1-2 mm (Srikanth, 2010). Drugs can be loaded onto the resins by an exchanging reaction, and hence, a drug-resin complex (drug resinate) is formed. Ion exchange can be defined as a reversible process in which ions of like sign are exchanged between liquid and solid, a highly insoluble body in contact with it. The drug is released from resinate by exchanging with ions in the gastrointestinal fluid, followed by drug diffusion. Being high molecular weight water insoluble polymers, the resins are not absorbed by the body and are therefore inert. Ion-exchange systems are advantageous for drugs that are highly susceptible to degradation by enzymatic process. A major advantage of ion exchange system is low running cost. It requires little energy and the regenerated chemicals are cheap (Srikanth, 2010). Cholestyramine resin USP, when used as an active ingredient, binds bile acids; this leads to replenishment of bile acids; through increased metabolism of serum cholesterol resulting in lowered serum cholesterol levels (Pande, 2011). Ion exchange resins no doubt are very effective in enhancing the bioavailability of the drugs but due to the utilization of some polymers it also enhances the cost of the delivery system.

**Nanosponge Drug Delivery:** Nanospheres are a new class of materials and made of microscopic particles with few nanometers wide cavities, in which a large variety of substances can be encapsulated. These particles are capable of carrying both lipophilic and hydrophilic substances and of improving the solubility of poorly water soluble molecules (Subramanian, 2012). This technology offers entrapment of ingredients and is believed to reduce side effects by controlling the release, improve stability, increase elegance and enhance formulation flexibility (Sharma and Pathak, 2010). These complexes can be also used to increase the dissolution rate and solubility, to mask unpleasant flavours and to convert liquid substances to solids. By controlling the ratio of polymer to the cross-linker the particle size and release rate can be modulated. Nanospheres enable the insoluble drugs and protect the active moieties from physicochemical degradation and controlled release. Atorvastatin, Fenofibrate, Glibenclamide, Glipizide, Lovastatin can be formulated into nanospheres (Subramanian, 2012).
Nanosponges improve the solubility of the drugs effectively but the technology employed in this process is not cost effective as this technique utilizes some polymers which are costly in nature.

**Nanoparticle Formulation:** Nanomaterials have unique physicochemical properties, such as ultra small size, large surface area to mass ratio, and high reactivity, which are different from bulk materials of the same composition. The use of materials in nanoscale provides unparalleled freedom to modify fundamental properties such as solubility, diffusivity, blood circulation half-life, drug release characteristics, and immunogenicity. As therapeutic delivery systems, nanoparticles allow targeted delivery and controlled release. Nanocrystalline fenofibrate Tricor is a clinically approved nanoparticle formulation (Zhang, 2008). Drug nanocrystals are the nanoparticles with a crystalline character. Drug nanocrystals are composed of 100% drug; there is no carrier material as in polymeric nanoparticles. Due to the poor aqueous solubility, instability and low bioavailability, Olea nolic Acid’s (OA) clinical applications are still limited. Recently, nanoparticulate drug delivery as the biological dimension of nanotechnology has been developed, which may help generate useful formulations of OA for clinical applications. Nanoparticulate drug delivery system enhances the dissolution rate and bioavailability of OA, providing a feasible formulation method for clinical applications (Chen, 2011).

**Mucoadhesive Microcapsules:** Oral route serves as the most convenient route for drug delivery. An ideal dosage regimen in the drug therapy of every disease is the one which maintains the desired therapeutic concentration of drug in the plasma for entire duration of treatment. An ideal oral controlled drug delivery system is one which delivers the drug at a predetermined rate, locally or systematically for a specified period of time (Kumar, 2012). Simvastatin (SV) is a cholesterol lowering agent that is derived synthetically from a fermentation product of *Aspergillus terreus* and is widely used to treat hypercholesterolemia. Microcapsules of Simvastatin were prepared by complexation with HPBCD and thereby including this complex in the polymeric matrix by use of orifice gelation technique resulted in more improved drug delivery (Bal, 2012).

**Buccoadhesive Drug Delivery System:** Bio adhesive systems are useful for the administration of drugs, which are susceptible to extensive gastrointestinal degradation and first pass metabolism, with short half-lives, requiring sustained and controlled delivery, with poor aqueous solubility. The buccal cavity provides a highly vascular mucous membrane site for the administration of drug. Buccal mucosa presents a relatively smooth and immobile surface for the placement of a bioadhesive dosage form (Gupta, 2011). The dosage forms developed for this purpose includes tablets, adhesive patches, adhesive gels, and adhesive ointment. Buccoadhesion is achieved by using various types of hydrophilic polymers. Lovastatin undergoes extensive first-pass metabolism in the liver and as a consequence of this the availability of Lovastatin in general circulation is very low and variable. The buccal formulation of Lovastatin in the form of buccoadhesive tablets was developed which increased the bioavailability of the drug (Doijad, 2011).

**Gastric Floating Drug Delivery System:** Floating systems or dynamically controlled systems are low-density systems that have sufficiently buoyancy to float over the gastric contents and remain buoyant in the stomach without affecting the gastric emptying rate for a prolonged period of time (Doijad, 2011). Fast GI transit prevents complete drug release in the absorption zone and reduces the efficacy of the administered dose since the majority of drugs are absorbed in stomach or the upper part of small intestine. Prolonging gastric retention of the dosage form extends the time for drug absorption. FDDS promises to be a potential approach for gastric retention. It also improves bioavailability, reduces drug waste, and improves solubility for drugs that are less soluble in high pH environment (Mayavanshi and Gajjar, 2008). Cellulose acetate butyrate (cab) - coated cholestyramine microcapsules as an intragastric floating drug delivery system endowed with floating ability due to the carbon dioxide generation when exposed to the gastric fluid. Cholestyramine microcapsules were distributed throughout the stomach and exhibited prolonged gastric residence via mucoadhesion (Umamaheshwari, 2003). Gastric floating drug delivery system of fenofibrate was prepared which showed improvement in the absorption and bioavailability (Lingarj, 2010).

**Pulsatile Drug Delivery System:** Pulsatile Drug Delivery System is useful in the diseases in which the drug release is timed to match rhythms of the disease so as to optimize the therapeutic effect and minimize the side effects. Circadian rhythm occurs during hepatic cholesterol synthesis which is higher during the night than daylight and diurnal synthesis represent upto 30-40% of daily cholesterol synthesis (Asija, 2012). However the maximal production occurs in the morning. So there is a constant need for new delivery systems that can provide increased therapeutic benefits to the patients by delivering drug at the right time, right place & in right amounts to coincide with circadian rhythm of body (Sukanya, 2012). These dosage forms offer numerous advantages, such as nearly stable plasma drug level without any fluctuations, reduction in dose of drug, reduced dosage frequency, least side effects, and improved patient compliance. Various systems like capsular system, osmotic system, and single multiple unit system based on the use of soluble or erodible polymer coating and use of repurtable membrane (Rasve, 2011; Rajput, 2012). Diseases where in PDDS are promising include asthma, peptic ulcers, cardiovascular ailments, arthritis and attention deficit syndrome in children and hypercholesterolemia (Parmar,
Statins are usually taken in one daily dose in the evening, presumably to coincide with cholesterol synthesis, which is thought to peak in the early morning hours. A pulsatile drug delivery of simvastatin was formulated which can be taken before bed time (9 pm) and capable of releasing drug after predetermined time delay (5 hours) and can characterized by proportioning drug concentration in the early morning hours when free cholesterol levels are more prevalent (Rasve, 2011).

CONCLUSION
In spite of extensive research and development of numerous drugs, antihyperlipidemic therapy is still deprived of the efficiency, safety, thorough knowledge of the exact mechanisms of the real causes of hyperlipidemia, and finally ‘cost’. The various novel drug delivery systems are employed to improve the solubility, bioavailability and effectiveness of anti hyperlipidimic drugs and the above explained systems are useful for the same. Nanoparticles, nanosuspensions and nanosponges are used to enhance the solubility of the drug by minimizing the particles size. Bucoadhesive and mucoadhesive drug delivery systems are employed to enhance the bioavailability of drugs that are degraded in the stomach by aiding the delivery of drug in buccal cavity where the vascular circulation is high.

Ternary solid dispersion and ion exchange resins are the systems which improve the solubility of drugs to a great extent and hence the bioavailability but it utilizes the various polymers which are costly in nature hence they may increase the cost of the medication. Gastric floating drug delivery system is helpful in improving the solubility of those drugs which are less soluble in acidic pH and the drug waste is much more. This system is helpful in prolonging the gastric retention of the drugs and therefore increases the solubility of the drugs. While as pulsatile drug delivery system is the system which responds to the circadian rhythms of the body and therefore this system is very effective because cholesterol synthesis depends on circadian rhythms. SMEDDS can be used to enhance the solubility of the drugs by decreasing the particle size in the emulsion base which will effectively increase the bioavailability of the drug.

Among all the systems above SMEDDS seems to be the most successful delivery system for antihyperlipidimic drugs because it is very easy to formulate and does not require any costly polymers which make it effective in therapy as well as in cost. Many other novel drug delivery systems can be used to enhance the effectiveness of these drugs.

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