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Review Article

NIOSOMES VERSUS PRONIOSOMES AS PROMISING DRUG DELIVERY SYSTEMS IN TREATMENT OF DIABETES MELLITUS

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ABSTRACT

Diabetes Mellitus (DM) has emerged as an epidemic that has affected millions of people globally in the last few decades. Conventional antidiabetic dosage forms have a lot of problems that necessitate searching for novel drug delivery systems to overcome these drawbacks. Niosomes and proniosomes have been used to carry a wide variety of antidiabetic drugs achieving controlled and sustained release, which improves patient compliance. This review article describes the fundamental aspects of niosomes and proniosomes, including their structural components, methods of preparation, advantages and drawbacks, characterization, factors affecting niosomes formation along with their application in the treatment of diabetes. It also highlights the participation of other drug delivery systems in the treatment of diabetes done, mainly in the last decade.

Keywords: Diabetes mellitus (DM), Niosomes, Proniosomes, Ethosomes, Nanoparticles

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INTRODUCTION

Diabetes Mellitus (DM) is a multi-factorial chronic pathological condition of elevated blood glucose level (BGL) caused by multiple genetic and/or environmental factors, more specifically due to either deficiency of secretion of insulin hormone or due to pancreatic β cells destruction. It may also be caused by the non-utilization of insulin due to insulin resistance (IR) [1, 2]. Diabetes mellitus (DM) is a major health issue, its prevalence presents a real threat to humans [3]. The possibility of diabetes varies in different ethnicities, such as black and Hispanic people, and some minorities, like American Indians and Natives of Alaska, are more likely to have diabetes for a specific genetic profile. Though a lot of antidiabetic drugs are present in the market, achieving a complete and successful cure for DM remains a problem as there are a lot of adverse effects associated with these medications like gastric irritation, phobia of injection, transient nausea, diarrhea, loss of appetite and many more. Also, frequent daily administration of conventional antidiabetic drugs leads finally to patient incompliance [4, 5]. Nanotechnology showed a promising role in the management of diabetes mellitus in the last few years. Vesicular drug delivery systems have gained wide attention in the field of nanotechnology. These systems have the potential to carry a variety of drugs and have been widely used for various goals such as drug targeting, controlled and sustained release, and enhancement of permeation for drugs with low permeability [6]. Nanotechnological systems overcome conventional dosage forms drawbacks such as low aqueous solubility, poor bioavailability, low membrane permeability, variable plasma concentration, undesirable effects, and of course, poor patient compliance because of multiple administration [7, 8].

Nanotechnological systems such as liposomes and niosomes can carry both hydrophilic and hydrophobic drug moieties by encapsulation and partitioning into hydrophobic and hydrophilic parts also act as drug reservoirs [9].

A lot of advantages, but some physical and chemical problems made liposomes unsuitable for oral administration, such as hydrolysis and degradation of phospholipids or problems associated with storage for a long time as aggregation, fusion or leakage, and oxidation in aqueous systems [10]. These drawbacks of liposomes opens the door for niosomes to make remarkable progress.

From the last decade onwards, Niosomes and proniosomes are used to improve oral bioavailability of antidiabetic drugs. Searched keywords include niosomes, proniosomes and diabetes mellitus. Sources include recently published review articles and papers mainly published in the last ten years. This review attempts to provide all the basic details about niosomes and proniosomes that were published mainly in the last decade. It focuses mainly on preparation methods of both niosomes and proniosomes, factors affecting their formation, characterization, advantages, disadvantages, and their application in the treatment of diabetes as well as the new achievements in other drug delivery systems to improve the treatment of diabetes. The next trend is using other nano drug delivery systems to improve bioavailability of antidiabetic drugs much more.

Types of diabetes mellitus (DM)

It is important to determine the type of diabetes to choose the right therapy. American Diabetes Association (ADA) sets the following classification [11]:

- Type 1 diabetes mellitus (T1DM) occurs due to autoimmune β-cell destruction, usually leading to absolute insulin deficiency.
- Type 2 diabetes mellitus (T2DM) occurs due to a progressive loss of β-cell insulin secretion frequently on the background of insulin resistance.
- Gestational diabetes mellitus (GDM) is diagnosed in the second or third trimester of pregnancy that was not overt before gestation.
- Specific types of diabetes due to other causes e. g., monogenic diabetes syndromes (such as neonatal diabetes and maturity-onset diabetes of the young (MODY)), diseases of the exocrine pancreas (such as cystic fibrosis and pancreatitis), and drug or chemical-induced diabetes (such as with glucocorticoid use, in the treatment of HIV/AIDS, or after organ transplantation).

The two main types are (T1DM) and (T2DM) [12]:

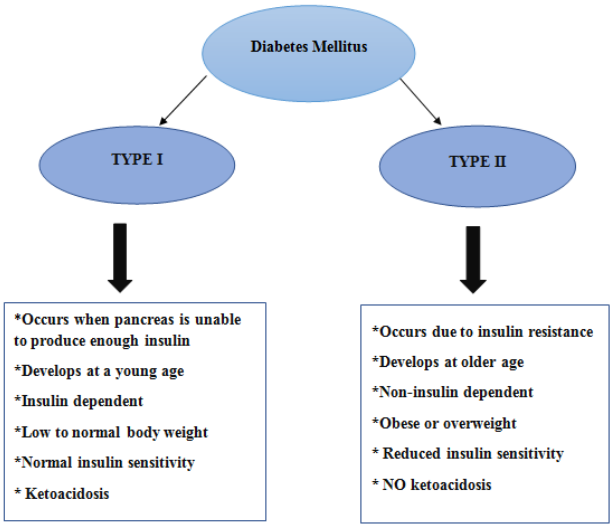

Fig. 1: Comparison between type 1 and type 2 diabetes mellitus [12]

There are many types of anti-diabetic drugs that exert their hypoglycemic effects via different mechanisms. The four major groups of anti-diabetic agents are [1]:

- Biguanides act mainly by reducing gluconeogenesis in the liver. The most known example of biguanides is Metformin which is the first-line oral drug of choice in the management of T2DM across all age groups. Metformin activates adenosine monophosphate-activated protein kinase in the liver, causing glucose uptake by the liver and inhibiting gluconeogenesis through complex effects on the mitochondrial enzymes [13].

- Insulin secretagogues include both meglitinides group, like repaglinide, and the sulfonylureas group. Their mechanism of action is increasing plasma insulin concentrations. Consequently, they can be used only when residual pancreatic β-cells are present. They rise plasma insulin levels by two mechanisms: the first mechanism is the stimulation of insulin secretion by pancreatic β-cells, the second one is decreasing insulin clearance by the liver [14].

- Insulin sensitizers, like thiazolidinediones for example, pioglitazone and rosiglitazone, have proven to be effective in improving the sensitivity of peripheral tissues to insulin, and also effective in hyperglycemia and lipid metabolism [15].

- Insulin or its analogs provide exogenous insulin in the form of recombinant insulin.

Niosomes components

Non-ionic surfactants

The most widely used non-ionic surfactants as niosomal drug delivery carriers are alkyl ethers and alkyl esters due to their availability and low issues of toxicity. They include Alkyl ethers such as (Brij) and alkyl esters as sorbitan fatty acid esters (Span) and polyoxyethylene sorbitan fatty acid esters (Tween). Cell culture toxicity studies have shown that niosomes composed of ester-type surfactants are less toxic than ether-type ones. This could be attributed to the possible enzymatic degradation of ester bonds [16]. These surfactants have been used in manufacturing niosomes with various routes of administration including nasal [17], oral [18], transdermal [19, 20], and ocular delivery [21–23].

Cholesterol (bilayer membrane stabilizer)

Cholesterol forms hydrogen bonds with hydrophilic surfactant heads in the bilayer structure of niosomes [19, 53]. Therefore cholesterol content affects niosomes structure and physical properties such as entrapment efficiency (E. E %), long time stability [24, 25].

Charge inducers

Aggregation is one of the most frequent physical instabilities of niosomes followed by fusion. Electrostatic stabilization of the niosomes can strongly suppress their aggregation [26]. Incorporation of positive and negative charge inducers in the bilayer membranes, such as Stearyl amine and dicetyl phosphate, can improve the physical stability of the niosomes against aggregation [16].

Niosomes consist of a bi-layered structure of non-ionic surfactants (fig. 2). When surfactants and cholesterol are mixed in a proper ratio and the temperature is above the gel liquid transition temperature, These thermodynamically stable bilayered structures are formed [27]. Depending on their size, these second-generation elastic vesicles can be divided into three types (fig. 3), small unilamellar vesicles (SUV) (10–100 nm), large unilamellar vesicles (LUV) (100–3000 nm), and multi-lamellar vesicles (MLV) in which more than one bilayer is present [28].

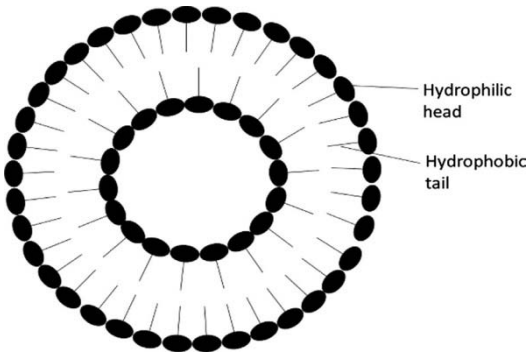

Fig. 2: Structure of niosomes [29]

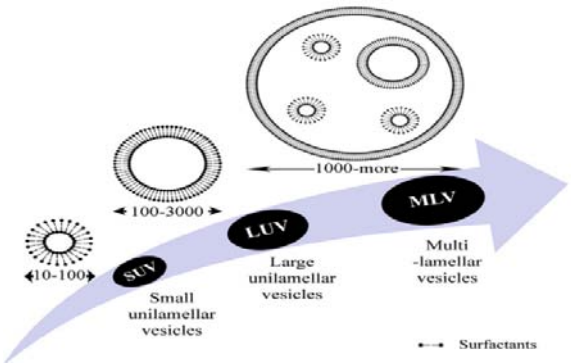

Fig. 3: Schematic structure of SUV, LUV, and MLV [30]

Advantages of niosomes

- Niosomes act as a reservoir to release the drug in a sustained pattern [31].
- They are biodegradable, biocompatible, and non-immunogenic, which made them an excellent choice [32].
- They can encapsulate large quantities of the drug in a relatively small volume of vesicles [33].
- Lipophilic drugs, hydrophilic drugs as well as amphiphilic drugs can be encapsulated in niosomes due to their unique structure [34, 35].
- Diverse administration routes (intravenous, oral, topical, etc.).
- In comparison with liposomes, Niosomes are more stable against chemical degradation or oxidation so they have a longer storage time [36].

Drawbacks of niosomes

- Physical instability problems such as aggregation, fusion, and leaking during storage and distribution, etc can be avoided by preparing proniosomes [37].
- The toxicity of the nonionic surfactants is not fully studied.
- Sterilization processes using heat, whether steam or dry heat sterilization, can cause bilayer destruction as the temperature exceeds the gel-liquid transition temperature of the surfactants, So the entrapped drug in the niosome bilayers leaked [38].
- Multilamellar vesicles preparation requires time and need specific tools [39].

Methods of preparation of niosomes

The widely reported preparation techniques are [40]:

Thin-film hydration (handshaking) technique

It is a simple technique; however, one of its disadvantages is that it involves the use of organic solvents to dissolve surfactants and cholesterol. In a round bottom flask surfactants and cholesterol are dissolved in chloroform or any suitable organic solvent followed by evaporation of that solvent to form a thin film on the bottom of the flask. That technique should be done at a temperature above the transition temperature of the surfactant. Hydration of this thin film produces multilamellar vesicles which are then sonicated to produce unilamellar vesicles [30, 41–44]. Niosomes prepared by this method have been reported to enhance the bioavailability of several anti-diabetic drugs, for example, repaglinide [45] and glimepiride [46].

Ether injection method

Both surfactant and drug are dissolved in diethyl ether and injected slowly through a needle with certain specifications to an aqueous phase, then heated above the boiling point of the organic solvent. This method produces large unilamellar vesicles (LUVs) and is further sonicated to obtain the required size [47–49].

Reverse phase evaporation method

Surfactants and cholesterol are dissolved in diethyl ether followed by the addition of the aqueous drug solution; then, the mixture was sonicated/homogenized. The organic layer was evaporated at room temperature under reduced pressure till niosomal suspension was formed [50, 51].

Trans-membrane pH gradient drug uptake process

In this method, both surfactant and cholesterol are dissolved in an organic solvent that is evaporated under reduced pressure, this leads to the formation of a thin film on the wall of the round bottom flask. This film is hydrated with citric acid and vortexed for a few minutes, so multilamellar vesicles (MLV) are formed. The resulting MLV are frozen and thawed thrice and then sonicated. Then aqueous phase is added and vortexed. The pH is adjusted finally to 7.0–7.2 by using disodium hydrogen phosphate. The resulting suspension is heated finally to 60 °C for 10 Min to obtain niosomes [26].

Emulsion method

Surfactants and cholesterol are dissolved in an organic solvent and then added to the drug previously dissolved in water. The formed emulsion is then heated to evaporate the organic solvent to obtain the niosomal formulation [52].

Bubble method

The most important advantage of this method is that it allows the preparation of niosomes without using organic solvents. In an aqueous phase, under a nitrogen atmosphere at 70 °C, Surfactants and additives are mixed. Mixing accomplished for 15s with high-speed homogenizer. In the last step, nitrogen bubbles are blown through the mixture at 70 °C to obtain niosomes as shown in fig. 4 [40, 53, 54].

Proniosome preparation

A lot of advantages are associated with this method, including rapid production process and ease of application. In this method, a water-soluble carrier is coated with a surfactant. Then the carrier is resolved during the hydration process at a temperature above the surfactant transition temperature, whereby niosomes are formed [55].

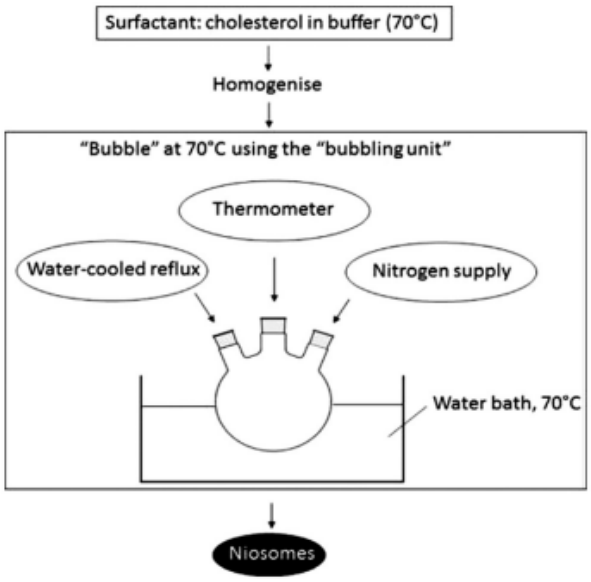

Fig. 4: Schematic diagram of bubble method [29]

Microfluidization method

This newly developed method produces smaller unilamellar vesicles with narrow size distribution. Across an interaction chamber, a solution of both drug and surfactants is pumped under a pressure rate of 100 ml/min [35]. This heat produced during microfluidization is removed by passing across a cooling loop to form niosomes [47].

Heating method

Both surfactant and cholesterol are hydrated separately in a buffer solution. After hydration, the cholesterol solution is heated for 1 h at 120 °C to be dissolved. Then the temperature of the solution is lowered, and surfactant and other additives are added to the buffer solution with continuous stirring. These formed niosomes are kept at room temperature for 30 min. Finally, niosomes are stored at 4–5 °C in a nitrogen atmosphere [24, 30, 56–58].

Proniosomes

Niosomal formulations show various advantages, such as improving the solubility and bioavailability of some poorly soluble drugs, as shown for acyclovir and griseofulvin, and maintaining good chemical stability during storage e. g. encapsulation increase the stability of peptide drugs [59]. Furthermore, low cost, more stability, ease of handling, formulation, and storage, less prone to oxidation make them a promising drug delivery system and superior to liposomes [13, 60]. On the other hand, Niosomes have some disadvantages which limit their shelf life, such as fusion, aggregation, sedimentation, leakage of entrapped drugs on storage, and loss of vesicular integrity [61–64].

To overcome all defects associated with niosomes, provesicular carrier systems are formulated i.e. anhydrous free-flowing proniosomal formulations. They can easily be reconstituted with the aqueous phase before administration or hydrated in body compartments to form niosomal vesicles (fig. 5) and these proniosomes-derived niosomes are more stable than conventional niosomes [65, 66].

Methods of preparation of proniosomes

There are different methods used for the preparation of proniosomes:

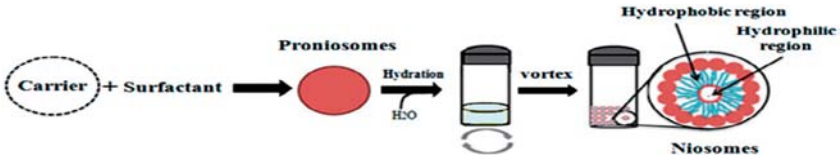

Fig. 5: Hydration of proniosomes into niosomes and hydrophilic and hydrophobic regions of niosomes [66]

Slurry method

This method includes Using carrier, surfactant, and organic solvent in a round bottom flask to obtain a slurry. The slurry is dried by applying vacuum to get free-flowing powder of proniosomes. The powder should be stored at 4 C in a sealed container [67].

Coacervation–phase separation technique

Previously determined amounts of both surface-active agent and cholesterol were mixed in glass vials. Small amount of absolute ethanol, typically half the weight of total lipids, enough to solubilize the lipids were added to the surfactant or surfactant/cholesterol mixture, and then, vials were tightly sealed and warmed in a water bath (55–60 °C) for 5 min while shaking until complete dissolution of lipids. To each of the formed transparent hot lipid solutions, an aqueous phase heated to 55–60 °C was added to the lipid solution while warming in the water bath for 3–5 min until a clear or translucent solution was produced. White creamy proniosomal gels were formed when the mixtures were allowed to cool down at room temperature [68].

Spray-coating method

This method involves the preparation of proniosomes by spraying surfactant/drug in an organic solvent onto a carrier or coating material and then evaporating the solvent [69].

Factors affecting niosomes formation

Type of surfactants used and charge inducers

Surfactants have a unique chemical structure which gives them dual properties. Nonionic surfactants are the main elements of niosomes. Various nonionic surfactants with different HLB values are used for the preparation of niosomes. The formation of niosomes and the encapsulation of drugs are influenced by the structure of surfactants. As the length of the alkyl chain of spans was increased, the entrapment efficiency of clarithromycin improved as reported by [70].

Addition of charge inducers

Adding some charge inducers such as dicetyl phosphate (negatively charged) and stearyl amine (positively charged) can stabilize niosomal formulations by imparting charge on niosomes surface, causing electrostatic repulsion, which prevents aggregation and coalescence [16, 30, 36, 39, 59].

Effect of encapsulated drug

An Important factor to be taken into consideration while formulating niosomes is the nature of the entrapped drug or in other words, the physicochemical characteristics of the drug. Drug characteristics such as molecular weight, structure, whether it is hydrophobic, hydrophilic, amphiphilic, etc. All of these factors have a great effect on both entrapment efficiency and the size of niosomes [71–73]. As reported in several articles, the maximum entrapment efficiency for a hydrophilic drug in niosomes could be between 10–20% [74, 75]. But in contrast, it was reported that entrapment efficiency of the hydrophilic drug (gallidermin, positive charge) in anionic niosomes could be up to 45% due to the interaction between niosomes negative charge and gallidermin positive charge [76].

Hydration medium

Hydration medium is one of the factors that greatly affects the properties of the prepared niosomes. Phosphate buffer is the most commonly used hydration medium. It can be used with various pH values according to the solubility of the entrapped drug [72, 77]. For example, zidovudine niosomes were prepared using phosphate buffer saline pH 7.4 [78]. Also, the temperature of the hydration medium is a critical factor as it affects both the size and shape of niosomes. It should be above gel to liquid phase transitional temperature [77, 79].

Hydration time

As said before, hydration medium influences the characteristics of the prepared niosomes. It was found that hydration time also affects the size and entrapment efficiency of niosomes. In a previously published article, results showed that short hydration time (15 min) resulted in vesicles (before the sonication step) with larger sizes and slightly less drug entrapment efficiency compared to niosomes subjected to a longer period of hydration (60 min) [80].

Characterization of proniosomes

Size and morphology

Scanning Electron Microscope and Transmission Electron Microscope can be used to determine surface characteristics, size,

and shape of niosomes. Formed proniosomes were spread on a glass slide and the structure of proniosomes was observed [81].

Charge of vesicle and zeta potential

The zeta potential of vesicles can indicate the stability of niosomes [82]. In general, concerning stability against aggregation and fusion, charged niosomes are generally more stable than uncharged vesicles [40]. Also, negative zeta potential values ranging between −41.7 and −58.4 mV are sufficiently high for electrostatic stabilization. Both surfactant type or encapsulation efficiencies might affect the zeta potential values. The zetasizer is used to determine surface zeta potential [30].

Entrapment efficiency

Entrapment efficiency can be expressed as the amount of drug incorporated into the niosomes and is normally defined as the percentage of niosomes bound drug to the total amount of drug added. Determination of the E. E% generally requires centrifugation of the preparation to separate free drug from the niosomes [83]. Determination of both entrapped and unentrapped drug allows calculation of entrapment efficiency. The entrapment efficiency can be calculated using the following formula [30, 84]:

$$\text{Percent entrapped} = \frac{[\text{Total drug}] - [\text{Free drug}]}{[\text{Total drug}]} \times 100$$

Stability study

Stability study discusses Storage feasibility of niosomal drug. One of the most important characteristics of a successful dosage form is the Stability of vesicles. There are a lot of factors that influence the Stability of niosomes such as nature of the entrapped drug, its concentration, type of surfactant used, and cholesterol amount. Stability studies investigate the percentage of drug leaching from niosomes during storage and while in general circulation. Using conditions that simulate both situations, this leaching can be evaluated by determining mean vesicle size, size distribution, and entrapment efficiency over several month periods. The stability of niosomes can also be assessed under conditions that accelerate photodegradation such as exposure to fluorescent light and UV irradiation as done for tretinoin niosomes [85]. It is important to provide chemical stability to both the surfactant and drug components so that the stabilization strategies must be optimized depending on the agent to be entrapped [30].

***In vitro* studies**

Depending on the administration route, *in vitro* release can be determined by inserting the niosomal suspension in a dialysis membrane and immersing it into a buffer at a definite temperature, and determining the content of the drug crossed into the buffer [30].

Table 1: Application of niosomes in improving bioavailability of antidiabetic drugs

Drugs	Type of formulation	Model	Results	References
Nateglinide	Proniosomal gel	*In vitro* release and *in vivo* study	Administration of nateglinide niosomal proconcentrate resulted in a rapid reduction in blood glucose level	[86]
Glimepiride	Proniosomal Gel	*In vitro* and *in vivo* studies	Improved entrapment efficiency	[87]
Pioglitazone	Niosomes prepared using span 20 and cholesterol	*In vitro* and *in vivo* studies in albino Wister rats	Maintain the drug at the site of treatment for a prolonged time, capable of supplying constant drug concentration for a longer duration as they sustain drug release	[88]
Repaglinide	Niosomes using span 60 and cholesterol	*In vivo* using male Wister rats	Increased repaglinide bioavailability which decreases dosing frequency from BID to OD	[89]
Metformin hydrochloride	Niosomes	*In vitro* *In vivo*	Prolonged drug release Improved anti-diabetic effect	[90]
Gliclazide	Niosomes	*In vivo*	Increased entrapement efficiency so that oral bioavailability was improved	[91]
Nateglinide	Proniosome powder	*In vivo*	Increased drug bioavailability	[92]
Glipizide and metformin hydrochloride Pioglitazone	Hydrogen bonded niosomes niosomes transgel	*In vitro* *In vivo*	Promising combinatorial sustained-release system Skin permeation increased Better bioavailability and antidiabetic activity	[93] [94]
Metformin	Niosomes using Spans/Tweens/Brijs with Cholesterol and dicetyl phosphate (DCP)	*In vitro* release studies with USP dissolution apparatus.	More stable vesicles, higher entrapment, and delayed-release formulation using span 60 with a longer chain length	[41]
Glipizide	Pronisomes using Span 60, cholesterol and coating agent either maltodextrin or sorbitol or mannitol	*In vitro* release	Using maltodextrin as a coating agent provides Consistent and prolonged release formula.	[41]
Metformin	Niosomes	*In vitro* release	Factors that lead to the best formula include 100 molar concentration of cholesterol and surfactant, Presence of DCP, an equimolar ratio of span 60: cholesterol, and 15 ml of hydration medium.	[95]
Metformin	Niosomes using either Span 60 or Span 40 or Tween 80 and cholesterol.	*In vivo*	Better sustained anti-diabetic effect than oral doses given daily.	[96]
Gliclazide	Niosomes using span 60 and cholesterol	*In vivo*	Cholesterol: surfactant ratio of 4:7 was found to achieve maximum entrapment of the drug. Additionally, the formulation showed good oral bioavailability of 89% *in vivo*.	[97]
Metformin	Niosomes using Span 40/cholesterol dicetyl phosphate and Dioleoyl-3-trimethylammonium propane (DOTAP)	*In vivo* and *in vitro*	The niosomal formulation showed a sustained release pattern which provides greater control of the hyperglycemic condition.	[90]
Pioglitazone	Niosomes using Cholesterol and span 20	*In vitro* and *in vivo* studies	The prepared formulation maintained steady drug concentration (sustained effect) for a longer duration of time, thereby enhancing the therapeutic action.	[98]

Tissue distribution and *in vivo* studies

To know the distribution pattern of a certain drug, animals are sacrificed and various tissues such as kidney, liver, lungs, and heart are removed, washed with a buffer then homogenized and centrifuged, and after that, the supernatant is analyzed for the drug content [59]. Concerning niosomes *In vivo* studies, they depend on the route of administration, drug concentration, the effect of the drug, and the presence time of the drug in tissues such as the liver and lungs [27].

Application of niosomes

Niosomes can be used efficiently for enhancing the bioavailability of the entrapped drug; several studies showed an increase in the bioavailability of several drugs as shown in table 1.

Applications of other nanotechnological systems in the treatment of diabetes mellitus

There are a lot of novel drug delivery systems that were developed to overcome the drawbacks of niosomes and to attain maximum bioavailability of antidiabetics, as shown in table 2 below.

Table 2: Application of different drug delivery systems in enhancing the bioavailability of antidiabetic drugs

Drugs	Type of formulation	Model	Results	References
Repaglinide	Ethosomes	Ex-vivo drug permeation study and *in vivo* study	Repaglinide ethosomes showed a prolonged antidiabetic action suggesting a sustained release from the transdermal formulation.	[99]
Linagliptin	Solid lipid nanoparticles (SLNs)	Pharmacokinetic and pharmacodynamic study	SLNs showed improvement in linagliptin bioavailability which may be due to P-gp efflux inhibition and lymphatic targeting.	[100]
Glimepiride	Nanosuspension prepared by combination technique and precipitation technique	*In vitro* drug release	The formulation prepared by combination technique showed good solubility, dissolution, and drug release in comparison with the formulation prepared by nanoprecipitation technique.	[101]
Repaglinide	Nanoemulsion	*In vivo* study	Repaglinide nanoemulsion showed a better hypoglycemic effect than tablet formulation.	[102]
Glimepiride	Self nano-emulsifying system	Ex vivo skin permeation study and *in vivo* study	It enhanced Glimepiride skin permeability and significantly lowered and controlled the blood glucose level in diabetic rats.	[103]
Gliclazide	Nanocrystal	*In vitro* drug release and *in vivo* studies	The nanocrystal formulation provided initial faster release followed by delayed release, which facilitate delivery of gliclazide and maintained the glucose homeostasis in T2DM patients with better therapeutic activity.	[104]
Metformin	Carbon Nanotubes	*In vivo* study	Metformin-conjugated nanotubes maintained a reduced blood sugar level for a longer time than metformin alone	[105]
Liraglutide	Polymeric Nanoparticles using poly (lactic-co-glycolic acid) [PLGA]	*In vitro* release study, permeability study, and enzymatic degradation study	Polymeric nanoparticles protected liraglutide from degradation in the gastrointestinal tract, it also improved intestinal permeability, which enhanced oral bioavailability of the drug.	[106]
Glibenclamide	Polymeric Nanoparticles using hydroxypropyl methylcellulose (HPMC)	*In vitro* dissolution	Glibenclamide-loaded NPs showed higher drug dissolution (85%) in comparison with pure drug (35%) and commercial preparation (56%) in 5 min.	[107]

CONCLUSION

In recent years, niosomes and proniosomes have attracted great attention in the field of nanotechnology. This attention is increasing because of their ability to encapsulate both lipophilic and hydrophilic drugs. Niosomes achieved great advancement in treatment of diabetes through improving bioavailability of antidiabetic drugs with flexibility in route of administration. The future direction goes towards using other nanovesicles like ethosomes, cubosomes, transferosomes, Solid Lipid Nanoparticles (SLNs), Nanostructured Lipid Carriers (NLCs), and surface-modified niosomes to achieve drug targeting, which enhance the bioavailability of antidiabetic drugs with minimization of adverse effects. All of these vesicular drug delivery systems need further exploration to achieve the required outcome.

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AUTHORS CONTRIBUTIONS

All authors have contributed equally.

CONFLICT OF INTERESTS

Declared none

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