SUMMARY AND CONCLUSION

To this day the most common form of delivery of drugs is the oral route. Even though this has the notable advantages of easy administration, it also has significant drawbacks namely poor bioavailability due to hepatic metabolism (first pass) and the tendency to produce rapid blood level spikes (both high and low), leading to a need for high or frequent dosing which are not only cost prohibitive and inconvenient but also unsafe.

In order to surmount these lacunae there is an urgent need for the development of Novel drug delivery system; which will improve the therapeutic efficacy and safety of drugs by more precise (i.e. site specific) spatial and temporal placement within the body, thereby reducing both the size and number of doses.

The increasing demand for efficient administration and delivery of Pharmaceutical dosage forms possessing the attributes namely minimum side effects, improved patient compliance has resulted in the formulation of novel drug delivery system. The revolutionary technology of drug delivery is off late being focused on the transdermal route in contrast to the conventional oral route. More over the bioavailability is poor and the onset of action is slow for most of the drugs which are sparingly suitable in water.

In the case of Carvedilol the oral route is preferred for the treatment of herpetic infections. However the inherent limitations namely poor absorption from the intestine (15-30%)

- Dose of administration (3.125 – 25 mg)
- Elimination half life (6 – 10 hrs.)
- Hypotension
- Bradycardia
- Weight gain
- Diarrhea
- Dizziness
- Asthenia

Hyperglycemias are glaring and limit this route of delivery of Carvedilol. Moreover this is irrational therapy viewing through the facets of Pharmaceopidemiology and Pharmacoeconomics.
Therefore there is a dire and urgent need to modify the route of administration. The most suitable route of administration is definitely the transdermal route. As the lipid layer is sizeable and its character is sizeable the penetration of Carvedilol through the transdermal route cannot be enhanced by the Liposome’s or Niosomes. Recent technological trends have been established to enhance the permeation by reducing the carrier size and making more malleable lipid layer in the form of novel medicament carrier as Ethosomes.

Ethosomes are very effective since they enhance the penetration of drugs via skin to several times whose compound to the simple creams, elixirs and liposomal carriers. Hence there is an absolute necessity to formulate Carvedilol as Ethosomes in order to increase the penetration of the drug through the skin. This would avoid the inherent defects of Carvedilol administrated via oral route by

- Reducing the frequency of administration
- Reducing the dose and this decreasing the toxicity
- Avoiding the adverse effects
- Providing better patient compliance.

In order to surmount these lacunae these is an urgent need for the development of Novel drug delivery system; which will improve the therapeutic efficacy and safety of drugs by more precise (i.e. site specific) spatial and temporal placement within the body, thereby reducing both the size and number of doses.

The most popular and often utilized method is the transdermal drug delivery system (TDDS) which means transport of the therapeutic substances through the skin for systemic effect. TDDS puts light on all topically administered drug formulations intended to the controlled and continuous delivery of the active ingredients in to the systemic circulation. The drug dosage form which adopts the novel technique is the transdermal patch. It is a medicament adhesive patch that is placed on the skin which directs the drug in to the blood stream. The drug is applied in relatively high dose to the inside of the patch which is worn on the skin for a extended period of the time. The principle underlying the TDDS is the process of diffusion which allows the drug to more from higher concentration area (Transdermal patch) to the blood stream until it attains the equilibrium. The diffusion in to the blood takes
place over a continuous period of time thereby maintaining a constant concentration of drug in the blood flow and thus ensures therapeutic efficacy.

The distinct advantages of TDDS are

- Avoids gastro intestinal drug absorption hassles caused by GI pH, enzymatic activity and drug interactions in the food.
- A very safe efficient and patient compliant alternative therapy to oral administrations of drugs especially in the case of vomiting and diarrhea.
- Avoid the first pass effect which is the initial passage of drug substance through the systemic and portal circulation subsequent to gastro intestinal absorption thereby also avoid the deactivation by digestive and liver enzymes
- Non invasive, avoiding the inconvenience of parenteral therapy.
- They provide extended therapy with a single application, improving compliance over other dosage forms requiring more frequent dose administration.
- The activity of drugs having standard short half-life is extended through the reservoir of drug in the therapeutic delivery system and its controlled release.
- Drug therapy may be terminated rapidly by removal of its application from the surface of the skin.
- They are easily and rapidly identified in emergencies (for example, unresponsive, unconscious, or comatose patients) because of their physical presence, features, and identifying markings.
- At the same time, transdermal drug delivery has few disadvantages that are limiting the use of transdermal delivery.

**Limitations of Ethosomes:**

- Poor yield
- If the locking is ineffective then the coalescence of Ethosomes may occur and they will fall apart on transfer into water.
- Loss of product during transfer from organic to water media.
The author keeping the mind the various problems confronted by patients being treated by the drug Carvedilol which is a anti hypertensive, adrenergic, adrenergic $\beta$ antagonist, vasodilator and adrenergic $\alpha$ antagonist agent which is indicated in the management of congestive heart failure (CHF), as an adjust to conventional ACE inhibitors and diuretics. Carvedilol provides additional mortality and mortality benefits in serve CHF. It is used in the treatment of chronic heart disease namely CHF and hypertension.

It has the lacunae namely

- Highly potent drug but possessing short half life.
- Very poor bioavailability (20-40 %) by oral route.

Investigated this research “DESIGN AND CHARACTERIZATION OF CARVEDILOL ETHOSOMES AS TRANSDERMAL DRUG DELIVERY SYSTEM”

In order to overcome all the lacunae and thus provide a therapeutically efficacious and unique dosage form. The distinct advantages of this formulation are that it does not cause Contact Dermatitis as in the case of transdermal patch.

Carvedilol is indicated in the management of congestive heart failure (CHF) as an adjunct to the conventional treatment by ACE inhibitor and diuretics. The use of Carvedilol has been shown to provide additional morbidity and mortality benefits in severe CHF and hypertension which needs prolonged treatment.

- To formulate and evaluate of Carvedilol Ethosomes.
- Induction of hypertension and measurement of hypertension.

At present, the most common form of delivery of drugs is the oral route. While this has the notable advantage of easy administration, it also has significant drawbacks- namely poor bioavailability due to hepatic metabolism(first pass) and the tendency to produce rapid blood level spikes(both high and low), leading to a need for high and or frequent dosing, which can be both cost prohibitive and inconvenient.

To overcome these difficulties there is a need for the development of new drug delivery system; which will improve the therapeutic efficacy and safety of drugs by more
precise (i.e. site specific), and spatial and temporal placement within the body thereby reducing both the size and number of doses.

One of the methods most often utilized has been transdermal drug delivery - meaning transport of therapeutic substances through the skin for systemic effect. Closely related is percutaneous delivery, which is transport into target tissues, with an attempt to avoid systemic effects.

The author keeping in mind the various problems confronted by the use of Carvedilol a antihypertensive agent, adrenergic agent, adrenergic beta antagonist, vasodilator agent, adrenergic alpha- antagonist is indicated in the management of congestive heart failure (CHF), as an adjunct to conventional treatments (ACE inhibitors and diuretics). The use of Carvedilol has been shown to provide additional morbidity and mortality benefits in severe CHF used in the treatment of chronic heart disease namely congested heart failure and hypertension which needs long treatment namely

- It is a highly potent drug with short half life.
- It has very poor bioavailability (20-40%) with oral route.

The author contemplated on this research work which is used for designing of Carvedilol Ethosomal gel containing various concentrations of ethanol, phospholipids and polymers by the cold method (sonication) for suitable size reduction of vesicles.

This research work involves the designing of Carvedilol Ethosomal formulations comparing various concentrations of Ethanol, phospholipids and polymers by the cold method (Sonicated) and cold method (Unsonicated) which facilitate the suitable size reduction of vesicles.

The preparation of Carvedilol Ethosomes involves the procedure as described. 20-40% of Ethanol, 10% of propylene glycol, 2-5% of phospholipids, 0-0.05g of cholesterol and an aqueous part of 100% w/w, were taken At room temperature 0.025g of Carvedilol was added to ethanol in a covered vessel along with propylene glycol and dissolved by vigorous stirring. In a separate vessel the mixture was heated to 30°C and this was added to the mixture in the centre of the vessel by stirring at 700 rpm for 5 min in a covered vessel. Then by Sonication method the vesicle size of Carvedilol Ethosomes was reduced to the desirable extent and the formulation was kept under refrigeration. The same procedure was followed
for the preparation of Unsonicated Ethosomes, except that they were not sonicated. Carvedilol Liposome’s were also prepared. They were prepared by the Cast Film method.

**Cold method:**

The widely and commonly used method for the preparation of Ethosomes is Cold method. While vigorous stirring dissolve the drug, phospholipids and the other lipid materials in ethanol in a vessel which is covered. Even add propylene glycol or any other poly glycol while stirring. Then heat the mixture in a water bath up to 30 degree C. In a separate vessel heat water up to 30 degree C and then stir it in a covered vessel for 5 minutes. Then by using either the extrusion method or probe sonication method the Ethosomal formulation's vesicle size can be modified to the desired extent.

**Characterizations of Liposomes:**

**Visualization:**

Liposomes can be visualized by using transmission electron microscopy (TEM) and microscopic electronic Scanning (SEM)\(^{51}\).

**Zeta potential and Vesicle size:**

Vesicle size and the zeta potential can be determined using photon correlation spectroscopy (PCS) and dynamic light scattering (DLS)\(^{52}\).

**Entrapment efficiency:**

By the use of ultra centrifugation technique the efficiency of entrapment of the drug by the Liposomes can be measured\(^{53}\).

**Transition temperature:**

Using differential scanning calorimeter the determination of transition temperature of the lipid systems of particles can be done\(^{54}\).

**Measurement of Surface tension activity:**

Surface tension activity of the drug in aqueous solution can be found by using Du Nouy ring tensiometer following ring method\(^{55}\).
Vesicle stability:

The stability can be determined by assessing size and structure of the particles. TEM is used to measure structure changes and DLS is used to measure mean size\textsuperscript{56}.

Penetration and permeation studies:

The depth of penetration of Liposomes can be visualised by (CLSM) Confocal-laser-scanning-microscopy\textsuperscript{57}.

Characterizations of Ethosomes:

Visualization:

By the use of scanning electron microscopy (SEM) and transmission electron microscopy (TEM) visualization of Ethosomes can be done\textsuperscript{51}.

Vesicle size and Zeta potential:

By the use of photon correlation spectroscopy (PCS) and dynamic light scattering (DLS) the size of the vesicle and the zeta potential can be determined\textsuperscript{52}.

Entrapment efficiency:

By the use of ultra centrifugation technique the efficiency of entrapment of the drug by the Ethosomes can be measured\textsuperscript{53}.

Transition temperature:

By the use of differential scanning calorimeter the determination of transition temperature of the lipid systems of particles can be done\textsuperscript{54}.

Surface tension activity measurement:

By the use of ring method in a Du Nouy ring tensiometer the activity of surface tension of the drug in aqueous solution can be done\textsuperscript{55}.

Vesicle stability:

By assessing the size and structure of the particles the stability can be determined. TEM is used to measure structure changes and DLS is used to measure mean size\textsuperscript{56}. 

Penetration and permeation studies:

By the use of (CLSM) Confocal laser scanning microscopy the depth of penetration can be visualised from ethosomes.\(^{57}\)

Applications of Ethosomes:

Pilo sebaceous Targeting:

In the percutaneous delivery of the drug sebaceous glands and hair follicles are found to have potential significance. Further a good amount of attention is being given on exploitation of the follicles as shunts of transport for systemic drug delivery. For pilosebaceous targeting the preparation and evaluation of monoxide formulation of Ethosomes was done by Maiden et al.\(^ {58}\)

Transdermal delivery of hormones:

When hormones are administered orally problems like low oral bioavailability, several side effects which are dose dependant and high first pass metabolism are observed and with each missed pill there is an increase in the risk of failure of treatment.\(^ {59}\)

Delivery of anti-parkinsonism agent:

Formulation of Ethosomes of trihexyphenidyl hydrochloride (THP) is done which is a psychoactive drug and comparison of its delivery with that of the liposomal formulation. THP is used in treating Parkinson's disease and it is a M1 muscarinic receptor. These results proved better potential of permeation of skin by Ethosomal THP formulation and that Parkinson's disease can be managed better by it.\(^ {60}\)

Transcellular delivery:

Ethosomes as an anti- HIV therapy is found to be an attractive clinical alternative when compared to the other formulations in the market.\(^ {61}\)

Topical delivery of DNA:

Through the skin many pathogens of the environment try to enter the skin. Skin is known as a protective barrier which has the ability to express the gene and also which is active immunologically. Based on the above facts use of Ethosomes to deliver DNA molecules topically in order to express the genes in skin cells is said to be an important
application. The possibility of usage of Ethosomes to deliver immunizing agents is due to the better ability of skin permeation of these dosage forms.

**Delivery of Anti-Arthritis drug:**

Anti-arthritis drug when delivered by topical route seems to have much prominence due to its site specific delivery and the problems which are found in conventional therapy are also overcome.

**Delivery of Antibiotics:**

To enhance the therapeutic efficacy of antibiotics delivery of the drug by topical route is the better option. Several side effects and allergic reactions can be seen in conventional oral therapy. Low permeability into the deeper skin layers and sub dermal tissues are possessed by conventional external preparations.

The designed Carvedilol Ethosomes will be characterized and validated by the parameters/ techniques namely visualization, Vesicle size and Zeta potential studies, Scanning Electron microscopy, Entrapment Efficiency, Assay, Vesicle stability study, Solubility measurement, Penetration and Permeation studies and drug stability studies.

Since the physical characterization is meant for physical integrity of the dosage form, the results were pooled at one place. Discussion on the results described for Sonicated and Unsonicated Ethosomes formulation and Liposome’s under the same heading as table which presented below.

**SIZE AND SHAPE ANALYSIS:**

Microscopic analysis was performed under different magnification to visualize the vesicular structure, lamellarity and to determine the size of Ethosomal and Liposomal preparations.

**ETHOSMES WITH SONICATION:**

Sonication method was adopted to reduce the vesicular size by giving high level energy to the lipid suspension. The type of Sonicator used was probe Sonicator in order to produce high energy to a small aliquot of the lipid suspension. The selected Ethosomal formulations were subjected to Sonication by the probe Sonicator. The photomicrograph
revealed that reduce the particle size of the Ethosomes after being subjected Sonication. The result of size and shape revealed consistency with the observations of Jain NK et al.,

**ETHOSMIES WITHOUT SONICATION:**

Ethosomes were prepared comprising of the formula containing 2-5% Phospholipids, 20-40% ethanol and quantity sufficient water were found to appear as multilamellar vesicles. It was observed that the Ethosomal lamellae were evenly spaced to the core. This confirms that the vesicular structure of high ethanolic concentration were present.

This Liposomal formulation was observed to be longer than that of Ethosomal formulation which were characterize to be multilamellar and gained type too.

Size distribution and average vesicular size analysis were done as per the procedure mentioned under methodology.

A comparative study of particle size distribution of Unsonicated and Sonicated Ethosomes was done. The data pertaining to this study is presented below as table below.

The results obtained by vesicular size analysis showed concentration of ethanol affect vesicular size. The size of Ethosomes decreased as the concentration of ethanol increased with the largest vesicles size 6.549 µm containing 20% ethanol and smallest 3.720 µm containing 40% ethanol.

Results obtained in the present investigation are in conformity with the results of Touitou E et al., 20007.

Microphotograph (figure 15-18) showed that size of the Ethosomes was reduced. The results of size and shape are consistent with the observations made by Jain NK et al.³.

Since the sizes of vesicles are reduced by Sonication, microscopic analysis followed previously to find the size distribution may not be satisfactory. Hence special software developed by “BIOVIS” was used to find the proper vesicular size distribution of the Sonicated products.

Result obtained here showed the maximum vesicular size is 6.549 µm for formulation containing 20% ethanol (EF4) and minimum is 3.720 µm for formulation containing 40% ethanol (EF6). Results obtained here are in same relation with concentration of ethanol.
When the results of particle size distribution of Sonicated and Unsonicated Ethosomes were compared and the data was compiled it revealed that the size of vesicles were 3.904 µm, 5.32 µm, 5.79 µm for Sonicated Ethosomes and 6.549 µm, 3.818 µm, and 3.720 µm for Unsonicated Ethosomes containing 20%, 30%, 40% and 20%, 30%, 40% w/w ethanol respectively.

The maximum entrapment efficiency of Ethosomal vesicles as determined by ultracentrifugation was 73.70% for Ethosomal formulation containing 20% ethanol (EF1) which was almost double to the formulation containing 40% ethanol (EF6). As the ethanol concentration increased from 20% to 40% w/w, there was decrease in the entrapment efficiency and with further increase in the ethanol concentration (>30% w/w) the vesicle membrane becomes more permeable that lead to further decrease in the entrapment efficiency.

Results of entrapment efficiency also suggest that 2% phospholipids is optimal concentration for entrapment efficiency and hence increased in concentration of phospholipids reduces the entrapment efficiency of vesicles. These results are further supported by observations made by Jain NK et al.\textsuperscript{14}

Entrapment efficiency of Ethosomal formulations is significantly different which are reported.

Increase in entrapment efficiency may be due to the possible reduction in vesicle size. The detrimental effect on the vesicle during ultra-centrifugation which are larger in size. Sonication gives the more uniform lamellae, smaller vesicle and uniform size and hence it may be the reason for higher vesicular stability and lesser vesicular disruption during ultra centrifugation.

Based on the in-vitro cumulative %drug release comparative studies of Carvedilol formulations it was established that EF2 (Sonicated Ethosomes) released maximum drug of 93.7%, EF3 (Sonicated Ethosomes) 89.3%, EF1 (Sonicated Ethosomes) 88.4%, EF4 (Unsonicated Ethosomes) 87.11%, EF5 (Unsonicated Ethosomes) 78.2%, EF6 (Unsonicated Ethosomes) 75.5%, EF gel 74.35%, liposome’s 72.44% followed by marketed drug FD 47.26%.

EF2 was adjudged the best based on in-vitro % drug release parameter which was almost two times the marketed drug.
RELEASE KINETICS:

The data of Carvedilol from different Ethosomes was processed to understand the linear relationship. The data were processed for regression analysis (Table-23). Using MS EXCEL statistical functions. The release kinetic of Carvedilol from all formulation followed zero order while release kinetic of aqueous solution and 20% ethanol in water values are far away from that of Ethosomal formulation. This is an encouraging observation.

STABILITY STUDY:

Ethosomal formulations were observed for any change in appearance or colour for a period of 8 weeks. There was no change in appearance in Ethosomal formulations throughout the period of study.

Even significance changes were not observed under the magnified view indicating that there was no increase in average size of vesicles for different formulation.. The stability of drug was further confirmed by spectral data and there was no change observed.

DRUG ENTRAPMENT AND DRUG CONTENT:

Since the stability of drug and stability of vesicles are the major determinant for the stability of formulation, studies were carried to evaluate total drug content at room temperature (27±2° C) and refrigeration temperature (4±2° C). Stability study could not be carried out at higher temperature (>room temperature) because phospholipids was used as the component for Ethosomes and gets deteriorated at higher temperature.

Loss in percentage of drug was not more than 4 percentages. Highest drug loss was observed at room temperature after 8 weeks as compared to refrigeration temperature. Results also showed that there was no significant change.

A comparative study of particle size distribution of unsonicated and Sonicated Ethosomes was done. The data pertaining to this study is presented below as table below.

The results obtained by vesicular size analysis showed concentration of ethanol affect vesicular size. The size of Ethosomes decreased as the concentration of ethanol increased with the largest vesicles size 6.549 µm containing 20% ethanol and smallest 3.720 µm containing 40% ethanol.
Results obtained in the present investigation are in conformity with the results of Touitou E et al., 20007.

Microphotograph (figure 15-18) showed that size of the Ethosomes was reduced. The results of size and shape are consistent with the observations made by Jain NK et al.³.

Since the sizes of vesicles are reduced by Sonication, microscopic analysis followed previously to find the size distribution may not be satisfactory. Hence special software developed by “BIOVIS” was used to find the proper vesicular size distribution of the Sonicated products.

Result obtained here showed the maximum vesicular size is 6.549 µm for formulation containing 20% ethanol (EF4) and minimum is 3.720 µm for formulation containing 40% ethanol (EF6). Results obtained here are in same relation with concentration of ethanol.

When the results of particle size distribution of Sonicated and unsonicated Ethosomes were compared and the data was compiled it revealed that the size of vesicles were 3.904 µm, 5.32 µm, 5.79 µm for Sonicated Ethosomes and 6.549 µm, 3.818 µm, and 3.720 µm for unsonicated Ethosomes containing 20%, 30%, 40% and 20%, 30%, 40% w/w ethanol respectively.

IN VIVO RELEASE STUDIES:

A deep analysis of the data obtained from the in-vivo release studies by the two methods namely the MPA induced hypertension and the sodium induced hypertension methods, the BP measurement studies have revealed that the EF2 formulation was the best when compared to EF4, EF7 and FD (marketed drug) formulation of Carvedilol.

These findings establish that EF2 (Sonicated Ethosomal formulation) elicited the best therapeutic activity of reducing the systolic blood pressure of the male Wistar albino rats. Hence it can be concluded that Sonicated Ethosomes of Carvedilol which have been designed by the author are highly efficacious for the treatment of congestive heart failure (CHF), hypertension, tachycardia and these are worthy of being patented.

In order to establish the identity of Carvedilol, various quantitative and qualitative analytical studies were performed namely scanning of Carvedilol by UV Spectroscopy at λmax 242 nm, FTIR studies to detect various functional groups of Carvedilol, and also
establish the purity of inactive ingredients viz Soya Lecithin, Ethanol, Cholesterol, Carbopol 934, Triethanolamine as well as the formulation Carvedilol Ethosomes.

The Carvedilol Ethosomal development can deliver the drug molecules into and in the skin. This research finding revealed that CEG is a highly efficacious formulation. The method of Touitou et al., was adopted with slightly modifications for preparing various formulations of Ethosomal constituting varied ethanol concentrations (20%- to 50%) by the technique of Sonication. The prepared Ethosomes were found to be discrete and spherical in shape.

The vesicle size was found to be between 3.26µm to 6.549 µm. The vesicles were observed to be small and uniform complying with the parameters of good skin penetration. The optimum formulation based on the bench marks of entrapment efficiency, transdermal flux, small vesicle size, uniformity, was chosen viz the Ethosomal prepared by using 20% w/w of ethanol by Sonication method.

Stability studies were carried out for duration of 8 weeks, and they revealed that the drug loss was not greater than 4%. Sonication has been proved to be a very efficient preparation method for Ethosomes of Carvedilol. Zeta potential determinations revealed good penetration of Carvedilol Ethosomes in to the skin.

The transdermal application of Carvedilol Ethosomal as a tremendous potential for commercial exploitation in the form of a patent. The research findings will further serve as standards for the Indian Pharma industry to scale up and develop a highly therapeutically efficacious Carvedilol Ethosomal formulation. The developed Carvedilol Ethosomal formulation is an excellent and safe dosage form for the treatment of congestive heart failure and hypertension, when compared to the Ethosomal gel, Liposome’s and the conventional Carvedilol market formulation.

Based on the in-vitro cumulative %drug release comparative studies of Carvedilol formulations it was established that EF2 (Sonicated Ethosomes) released maximum drug of 93.7%, EF3 (Sonicated Ethosomes) 89.3%, EF1 (Sonicated Ethosomes) 88.4%, EF4 (Unsonicated Ethosomes) 87.11%, EF5 (Unsonicated Ethosomes) 78.2%, EF6 (Unsonicated Ethosomes) 75.5%, EF gel 74.35%, liposome’s 72.44% followed by marketed drug FD 47.26%. EF2 was adjudged the best based on in-vitro % drug release parameter which was almost two times the marketed drug.
A deep analysis of the data obtained from the in-vivo release studies by the two methods namely the MPA induced hypertension and the sodium induced hypertension methods, the BP measurement studies have revealed that the EF2 formulation was the best when compared to EF4, EF7 and FD (marketed drug) formulation of Carvedilol. These findings establish that EF2 (Sonicated Ethosomal formulation) elicited the best therapeutic activity of reducing the systolic blood pressure of the male Wistar albino rats. Hence it can be concluded that Sonicated Ethosomes of Carvedilol which have been designed by the author are highly efficacious for the treatment of congestive heart failure (CHF), hypertension, tachycardia and these are worthy of being patented.

RECOMMENDATIONS:

1. As the Carvedilol Ethosomes have been prepared by the cold method which is the most simple and economical method when compared to others, it is recommended that this process of manufacturing can be adopted as a routine procedure by the Pharmaceutical Industry.

2. When compared to the conventional dosage forms available in the market namely tablets, injections, Carvedilol Ethosomes prepared by the author have many advantages in addition to enhancing the bioavailability. Hence it is recommended that Carvedilol Ethosomes be prepared instead of conventional dosage forms for the treatment in patients suffering from CHF Hypertension and Tachycardia.

3. Carvedilol Ethosomes are recommended keeping in view the excellent patient compliance.

4. Carvedilol Ethosomes are to be used in the place of Liposomes since they have many disadvantages namely high production cost, leakage, fusion of encapsulated drug, low stability due to hydrolysis and oxidation reactions.

5. Safety of the formulation from the angle of pharmacovigilance is ensured since all the raw materials used are non toxic.
6. Since the use of Ethosomes doesn’t involve any invasion pain or distress, Carvedilol Ethosomes are recommended for their intended use.