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Nanostructured Lipid Carriers As A Drug Delivery System

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ABSTRACT

Nanostructured Lipid Carriers (Nlcs) Are Drug Delivery System Comprising A Mixture Of Solid And Liquid Lipids As A Core Matrix. Furthermore, Nlcs Are Second-Generation Lipid Nanoparticles That Have An Unstructured Matrix With High Drug Loading Capacity, Which Are Suitable For Drug Delivery System. Due To These Unique Characteristics, Several Studies Have Investigated Nlcs As Alternate Carriers For The Dermal Delivery Of Pharmaceuticals, Particularly Natural Active Ingredients. Among The Associated Benefits Discovered Include Biocompatible Ingredients, Drug Release Modification, And Adhesion To The Skin, Film-Forming Ability With Hydration Of The Superficial Skin Layers, As Well As Increased Penetration And Permeation Into Deeper Skin Layers. Nlc It Can Be Easily Used As A Carrier For Drugs Via Different Routes Of Administration Such As Oral, Parenteral, Ocular, And Nasal. Nanostructured Lipid Carriers (Nlcs) Have Been Reported To Be An Alternative System And Are Considered Superior To Many Other Traditional Lipid-Based Nanocarriers Such As Emulsions, Nanoemulsion, Liposome, Microparticle, And Solid Lipid Nanoparticle (Slns). It Imparts Many Advantages Over Sln's Such As Increased Solubility And Stability, Improved Permeability And Bioavailability, Enhanced Drug Loading Capacity, Drug Release Modulation Flexibility, Reduced Adverse Effects, Prolonged Half-Life, And Tissue-Targeted Delivery. This Review Highlights The Nlc With A Focus On The Structure ,Pharmaceutical And Therapeutic Applications Towards Targeted Drug Delivery Of Nlc In Delivery Systems.

Keywords: *Drug , Nanostructured Lipid Carriers (Nlc) , Thermodurmal , Nanotechnology , Nateglinide*

1. INTRODUCTION

Over The Last 20 Years, Nanotechnology Has Practically Made Its Influence In All Technical Fields, Including Pharmaceutics. Industry Estimated That Approximately 40% Of Lipophilic Drug Candidates Fail Due To Solubility And Formulation Stability Issues, Which Has Been Solved By Various Novel And Advanced Lipophilic Drug Delivery Technologies. The Lipids Employed To Prepare Lipid Nanoparticles Are Usually Physiological Lipids With Low Acute And Chronic Toxicity. In Recent Years, Solid Lipid Nanoparticles (Slns) Have Garnered Great Importance As Potential Drug Carriers For Oral Delivery Due To Their Unique Advantages And Great Versatility As Compared To Polymeric Nanoparticles, Nanoemulsions, Liposomes. The Slns Are Made Of Solid Lipid Material, Which Remains In The Solid State At Room Temperature, Protects The Chemically Labile Drugs, And Provides Slow Drug Release To Achieve Controlled Drug Release Profiles For Prolonged Time Intervals. Nanostructured Lipid Carrier (Nlc) Is Second Generation Smarter Drug Carrier System Having Solid Matrix At Room Temperature. This Carrier System Is Made Up Of Physiological, Biodegradable And Biocompatible Lipid Materials, Surfactants And Is Accepted By Regulatory Authorities For Application In Different Drug Delivery Systems. Nlc Exhibit Superior Advantages Over Other Colloidal Carriers Like Nanoemulsions [1], Polymeric Nanoparticles, Liposomes, Sln Etc. And Thus, Have Been Explored To More Extent In Pharmaceutical Technology. The Whole Set Of Unique Advantages Such As Enhanced Drug Loading Capacity, Prevention Of Drug Explosion Leads To More Flexibility For Modulation Of Drug Release And Makes Nlc Versatile Delivery System For Various Routes Of Administration. Nlc Has Pharmaceutical Applications For The Various Routes Of Drug Delivery Like Topical, Oral, Pulmonary, Ocular And Parenteral Administration And Its Future Perspective As A Pharmaceutical Carrier.Natural Ingredients Can Be Loaded Into Nano Lipid Carriers To Create Advanced Product Formulation In Numerous Techniques And Systems. These Include High-Pressure Homogenization (Hph), High-Shear Homogenization Followed By Ultrasonication, Microemulsion, Solvent Emulsification/ Evaporation, Membrane Contactors, Phase Inversion (Separation), And Coacervation[2]

Different Types Of Nlcs

- **Type 1 Nlcs (Imperfect)**

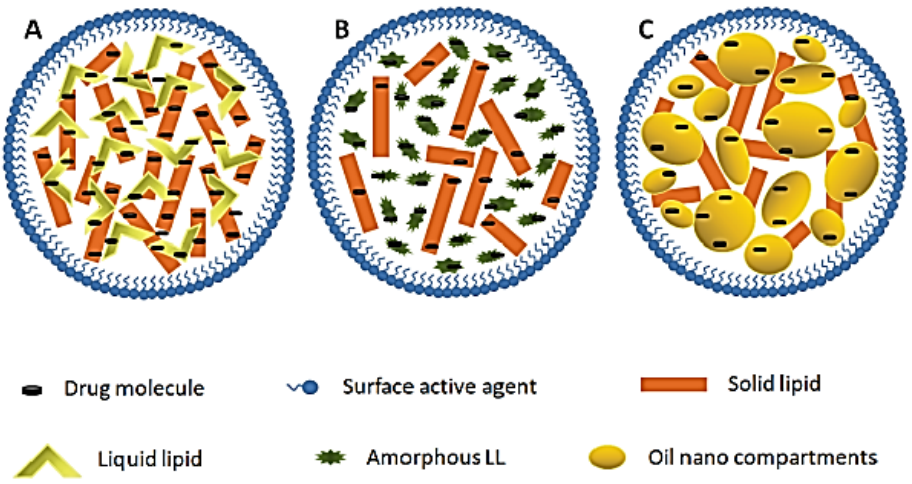
Type I Nlcs Have An Imperfect Crystal Core Structure Due To The Partial Replacement Of A Portion Of Solid Lipid With Liquid Or Oil. Moreover, This Type Has A High Loading Capacity And Excellent Drug Release Profiles.

- **Type 2 Nlcs (Amorphous/Structure Less)**

Mixing Solid Lipids With Specific Lipids That Stay In A Polymorph After Solidification Leads To The Production Of Type 2 Nlcs. The Use Of Medium-Chain Triglycerides, Hydroxyoctacosanyl, Hydroxy Stearate, Or Isopropyl Myristate In Conjunction With Solid Lipids Has Been Found To Yield The Desired Outcome. This Type Is Generally Preferred Due To The Absence Of Crystallization And The Drug Remains Incorporated In The Amorphous Matrix. Consequently, Drug Release Induced By The Crystallization Process To B Forms During Storage Can Be Avoided [3]**.**

- **Type 3 Nlcs (Multiple)**

Type 3 Nlcs Are Conceptually Developed From W/O/W Emulsion. When The Loaded Drug Has High Oil Solubility, This Method Can Be Used To Formulate Nlcs With Increased Loading Capacity And Stability. In This Method, Small Droplets Of Oil Are Consistently Dispersed Throughout A Solid Lipid Matrix In An Aqueous Phase.



Different types of NLCs.
(A) Imperfect: (B) Amorphous: and (C) Oil-in-fat-in-water

Figure Error! No text of specified style in document. **Morphological Models Of Different Types Of Nanostructured Lipid Carriers (Nlcs).**

Role Of Nlc In Transdermal Drug Delivery

Transdermal Drug Delivery System Is An Established System Since Ages To Attain Diverse Therapeutic Objectives On Different Structural Levels Of Skin (E.G. Surface, Epidermis, Dermis And Hypodermis). However, Several Problems Associated With The Conventional Topical Preparations Have Come In Picture E.G. Impermeability To Skin Barrier, Limited Efficacy And High Frequency Of Application.[4] The Current Focus Of The Researcher Is Quite Related Towards Exploiting Nlc For Topical And Dermal Application, Both In Pharmaceutical As Well As Cosmetic Sector. Nlc Are Composed Of Biologically Active And Biodegradable Lipids That Show Less Toxicity And Offer Many Favorable Attributes Such As Adhesiveness, Occlusion, Skin Hydration, Lubrication, Smoothness, Emolliency, Skin Penetration Enhancement, Modified Release, Improvement Of Formulation Appearance Providing A Whitening Effect And Offering Protection Of Actives Against Degradation. The Key Advantageous Features Offered By Nlc That Makes Its Role Superior In Transdermal Drug Delivery Are As Follows

Objectives

- ✓ To Study Role Of Nlc In Transdermal Drug Delivery
- ✓ To Study Effect Of Nateglinide Formulations On Blood Sugar

- ✓ To Study Calibration Curve For Nateglinide Pure Drug (Hplc)
- ✓ To Study Ex-Vivo Skin Permeation Studies Of Nateglinide Nlc Loaded Transdermal Patches
- ✓ To Study Solubility Of Nateglinide In Various Lipids

2. REVIEW OF LITERATURE

Khaled (2022)[5] This Article Summarize The Development Of A Nanostructured Lipid Carrier (Nlc) Of Sesame Oil (So) Loaded With Miconazole (Mz) That Could Overcome The Solubility Problems Of Mz And Enhance Its Antifungal Activity Against Oral Candidiasis. In The Formulation Of This Study, So Was Used As A Component Of A Liquid Lipid That Showed An Improved Antifungal Effect Of Mz. An Optimized Mz-Loaded Nlc Of So Was Used, Based On A Central Composite Design-Based Experimental Design; The Particle Size, Dissolution Efficiency, And Inhibition Zone Against Oral Candidiasis Were Chosen As Dependent Variables. A Software Analysis Provided An Optimized Mz-So Nlc With A Particle Size Of 92 Nm, Dissolution Efficiency Of 88%, And Inhibition Zone Of 29 Mm. Concurrently, The Ex Vivo Permeation Rate Of The Sheep Buccal Mucosa Was Shown To Be Significantly ($P < .05$) Higher For Mz-So Nlc As Compared With A Marketed Mz Formulation (1215 µg/Cm2) And An Aqueous Mz Suspension. Additionally, An In Vivo Efficacy Study In Terms Of The Ulcer Index Against C. Albicans Found A Superior Result For The Optimized Mzso Nlc (0.5 ± 0.50) In A Treated Group Of Animals. Hence, It Can Be Concluded That Mz, Through An Optimized Nlc Of So, Can Treat Candidiasis Effectively By Inhibiting The Growth Of C. Albicans.

Lala Et Al (2020)[6] Formulated & Characterized The Nlc Formulation Loaded With Dolutegravir For The Solubility Enhancement And Permeability Improvement Through The Intestine. For This Work, Gelucire 50/13, Dynasan 118 & Gms As Sl, Capmul Mcm (Ll) And Tween 80 & Span 80 Were Used As Surfactants For Formulation Preparation. Response Surface Methodology Was Used For Formulation Optimization. The Ps, Zp & Pdi Result Shows 123.1 Nm, -16.1 Mv, And 0.406 Respectively. In-Vitro Drug Release Of Nlc Formulation Shows (96.32 % In 48 H) And The Drug Permeability Through The Intestine Of Rat Model Shows 94.02% In 8 H. The Flux Of Drug Suspension & Nlc Loaded Drug Shows 0.254 Mg/Cm2 Hr, And 8.73 Mg/ Cm2 Hr. Respectively. Hence It Was Confirmed For The Experiment That The Nlc Carrier Was Better Compared With Only Drug Suspension For Improving Solubility And Permeability.

Hassan Et Al (2019)[7] Formulate & Evaluate The Olmesartan Drug-Loaded Sln & Nlc For Better Treatment Of Hypertension. To Prepare The Formulation, Hsh With Ultrasonication Method Employed. The 23 Full Factorial Designs Were Used To Optimize The Formulation. The Same Drug Of Two Different Formulations Was Prepared. Here Gms & Oleic Acid Was Used As Sl & Ll Respectively. Tween 80 & Poloxamer 188 Were Used As Surfactants With A Concentration Of 0.25-5%. The Formulation Shows Ps Of 219.9 To 363.5 Nm And 176.8 To 382.2 Nm For Sln & Nlc Respectively. The Ee Of The Drug In The Formulation Was Found 84.55 % & 90.64 For Sln & Nlc Respectively. The Drug Release From Sln & Nlc Loaded With Olmesartan Was Found Sustained Release. Compared With Both Carriers Nlc Was Found Better & Potential Carrier For Formulation Design & Evaluation Of Olmesartan For Treatment.

Panda And Kuotsu (2019)[8] Carried Out Research Work For Cancer Treatment Using Nlc-Loaded Methotrexate. The Formulation Components Included Monostearin (Sl), Olive Oil & Pegylated Glyceride Labrasol (Ll), And Poloxamer 188 (Surfactant). The Hot Melt Emulsification & The Probe Sonication Was Used For The Production Of Nlc. The Prepared Formulation Was Subjected To Various Physicochemical Analysis & Cytotoxicity Studies. The Result Shows That The Average Ps From 112.1±5.6 To 199.6±1.7 Of Blank Nlc & Drug-Loaded Nlc. The Zp Was Found −28.5±77 Mv For Drug Loaded Nlc. The Ee% Was 95. 24 Indicate Good Entrapment Efficiency. Depending On The Type Of Liquid Lipid In Formulation The In-Vitro Drug Release Was From 66.45% To 94026% After 8 H. In Vitro, Cytotoxicity Shows That Mtx-Nlc Significantly Produce More Cytotoxic Effect In Comparison With Mtx Solution And Mtx-Nlc Olive Oil Formulation. The Stability Study Indicates That The Formulation Was Stabilized (Room-Temperature Storage Shows More Ps Compared With Refrigerator Storage). The Overall Result Indicates That Nlc Was A Good Carrier For The Effective Delivery Of Drugs.

Yin Et Al., (2017)[9] This Article Provide Information Related Development Of Selenium Coated Nanostructured Lipid Carriers For Enhancing The Oral Bioavailability And The Curative Effect Of Berberine, An Antidiabetic Phytomedicine. Berberine-Loaded Senlcs Were Prepared By Hot-Melt Dispersion/Homogenization Procedure Followed By In Situ Reduction. Bb-Senlcs Were Characterized By Particle Size, Morphology, Entrapment Efficiency (Ee) And In Vitro Release. Pharmacokinetics Of Berberine Solution, Berberine-Loaded Nlcs And Bb-Senlcs Were Studied In Sprague Dawley Rats Administered By Oral Gavage. The Prepared Bb-Senlcs Were Around 160 Nm In Particle Size With An Ee Of 90%. In Addition, Bb-Senlcs Exhibited A Better Sustained Release Of Berberine Compared To The Plain Nlcs. After Oral Administration, Bb-Senlcs Greatly Enhanced The Oral Bioavailability Of Berberine, Which Was Approximately 6.63 Times As Much As That Of Berberine Solution. The Hypoglycemic Effect Of Bb-Senlcs Was Also Significantly Superior To That Of Bb-Nlcs And Berberine Solution. It Turned Out That Sustained Drug Release And Good Intestinal Absorption, Plus The Synergy Of Selenium, Was Basically Responsible For Enhanced Oral Bioavailability And Hypoglycemic Effect. Findings Show That Senlcs Are Promising Nanocarriers For Oral Delivery Of Berberine To Strengthen The Antidiabetic Action. Andres Felipe

Wei Keat Ng Et Al. (2015)[10] Developed Thymoquinone (Tq) - Loaded Nanostructured Lipid Carrier (Tq-Nlc) To Improve The Bioavailability And Cytotoxicity Of Tq On Breast Cancer (Mda-Mb-231 And Mcf-7) And Cervical Cancer Cell Lines (Hela And Siha). Tq-Nlc Was Prepared By Applying The Hot High Pressure Homogenization Technique Yields In Mean Particle Size Of 35.66 ± 0.1235 Nm With A Narrow Polydispersity Index (Pdi) Lower Than 0.25. The Zeta Potential Of Tq-Nlc Was Greater Than −30 Mv. Polysorbate 80 Helps To Increase The Stability Of Tq-Nlc. The Encapsulation Efficiency Of Tq In Tq-Nlc Was 97.63 ± 0.1798% As Determined By Hplc Analysis. Tq-Nlc Exhibited Antiproliferative Activity Towards All The Cell Lines In A Dose-Dependent Manner Which Was Most Cytotoxic Towards Mda-Mb-231 Cells.

Keshri Et Al. (2013)[11] Developed Topical Delivery System Of Nanostructured Lipid Carriers (Nlc) Of Econazole Nitrate (En) For The Treatment Of Deep Seated Fungal Infection By Improving Its Permeability. Fifteen Formulations (F1-F15) Of Nlcs Were Prepared And Characterized. Five Nlc Optimized Formulations Were Formulated As Hydrogels (G1-G5) Using Carbopol 934. Confocal Laser Scanning Microscopy Demonstrated Penetration Of Rhoda Mine Red Till The Stratum Basale Due To Hydration Of Stratum Corneum. Hydrogel G3 Containing Nlc Formulation (F5) Was Selected As The Optimized Topical Gel. Transmission Electron Microscopy (Tem) Of F5 Revealed Spherical Particles. Stability Profile For 90 Days Revealed Insignificant Change In The Particle Size And Zeta Potential Indicating Substantial Stability Of The System.

Xia Et Al. (2012)[12] Developed A-Lipoic Acid Loaded Nanostructured Lipid Carriers (Alanlc) By High Pressure Homogenization (Hph) Technology. The Effects Of Polymer Surfactant Emulsifying Agents On The Formation And Stability Of Ala-Nlc Were Characterized By Dynamic Light Scattering (Dls), Rheological Analysis, Wide Angle X-Ray Diffraction (Waxd), And High Efficiency Liquid Chromatography (Hplc). The Particles Size, Viscoelastic Property And Stability Of Ala-Nlc Samples Were Significantly Influenced By Polymer-Surfactant Emulsifying Agents. Polymer Is Considered As A Primary Emulsifying Agent In Ala-Nlc. Surfactants, Which Have Small And Flexible Hydrophilic Head Group, Would Have Strong Interaction With Polymer, And Form Strong Interfacial Film, Thus Could Improve The Stability Of Ala-Nlc. These Results Will Be Productive For Better Understanding Of The Preparation And Stability Of Nlc.

3. RESEARCH METHODOLOGY

Research Methodology Is A Way To Systematically Solve The Research Problem. It May Be Understood As A Science Of Studying How Research Is Done Scientifically. In It We Study The Various Steps That Are Generally Adopted By A Researcher In Studying His Research Problem Along With The Logic Behind Them. It Is Necessary For The Researcher To Know Not Only The Research Methods/Techniques But Also The Methodology.

In Order To Apply The Analytical And Descriptive Methods To The Research A Close Reading And Detailed Analysis Of Secondary Sources Available.It Is Significant To Get Other Perceptions To Elaborate The Textual Analysis And This Would Need Close Reading Analysis Of Few Secondary Materials.

4. RESULT AND DISCUSSION

The Solubility Studies Are Carried Out By Using Shake Flask Method Under Isothermal Condition. The Solubility Studies For Both The Drugs Were Determined By Using Various Lipids. Nateglinide Showed Low Solubility In Water And High Solubility In Lipids Like Witepsol, Compritol And Stearic Acid.[13]

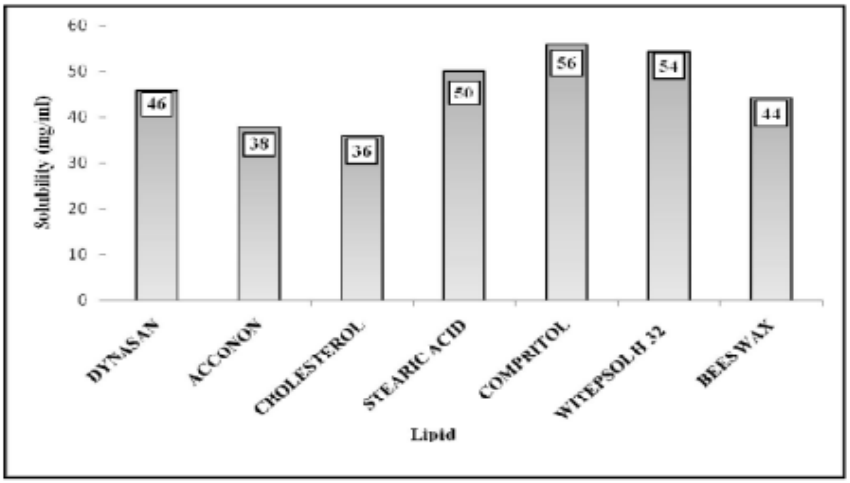


Figure 1 Solubility Of Nateglinide In Various Lipids

The Formulated Nlc Transdermal Patches Were Characterized For Weight Variation (Mg/Cm 2); Thickness (Mm); Folding Endurance; % Moisture Content; % Drug Content; Ex-Vivo Skin Permeation Studies For 48 Hrs. By Franz Diffusion Cell;

Invitro Release Kinetic Studies Like Zero Order Kinetics Studies; First Order Kinetics Studies; Higuchi Kinetic Model; Hixson Crowell Kinetic Model; Korsmeyer Peppas Kinetics Model. The Individual Weight Of The Patch For All The Formulations Has No Deviation From The Average Weight; It Shows A Uniformity Of Weight Of Each Patch Which Leads To The Encapsulation Of Drug Content All Over The Batch. While Measuring The Patch Thickness In Three Different Places Of The Patch, It Showed Uniformity Of Thickness All Over The Patch, Which Implied Good Flatness Of The Patch And Also It Confirmed That There Was No Accumulation Of Polymer Content At A Particular Place Of The Patch With More Thickness. Formulation Nt4 Shows Good Folding Endurance Of 80-90 When Compared To All Other Patches Which Reflected The Desired Concentration Of Plasticizer And Good Elasticity Of Patch. The Moisture Content For All The Formulations Was Found To Be<1 %, Which Indicated That There Was No Interaction Of Moisture In Patch; It Has Good Stability On Long Term Storage And Also It Will Be Away From Microbial Contamination. The Percentage Drug Content For Nt4 Formulation Was Found To Be More I.E., 95.42±0.75% When Compared To All Other Formulations. This Implies That By Increasing The Concentration Of Polymer Proportion The Nlc Entrapment In Patch Also Increased, Which In Turn Increased The Drug Content. The Ex-Vivo Drug Permeation Studies Through Rat Skin For The Optimized N16 Nateglinide Nlc Loaded Transdermal Patch Formulation (Nt1-Nt4) Was Carried Out In Ph 7.4 Phosphate Buffer By Using Franz Diffusion Cell.[14] The Percentage Amount Of Drug Permeated Through The Rat Skin Was Found To Be 95.48 ± 3.22% To 99.48 ± 4.02% In 48 Hr. From The Results It Was Observed That, Nt4 Nlc Transdermal Patch Showed Better Control Of Drug Release With Good Permeation Index. In General, The Drug Release From Nt4 Formulation Showed A Predetermined Control Of Release Which Obeyed Zero Order Drug Release Pattern.

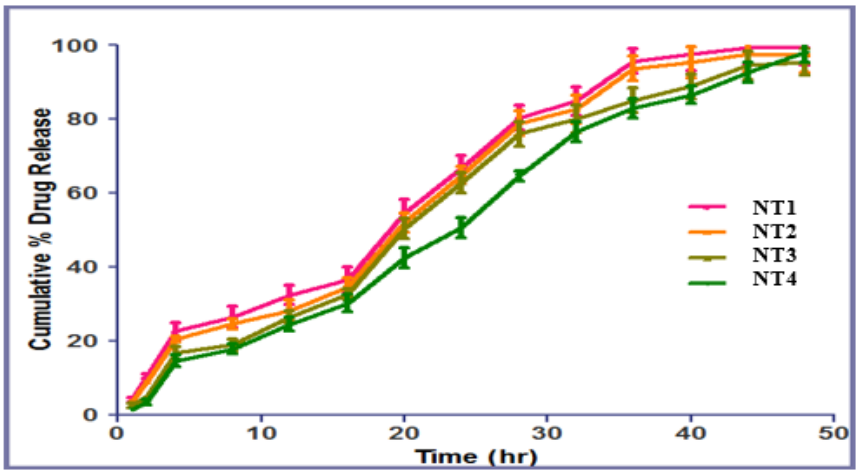


Fig. 3 Graph Showing Ex-Vivo Skin Permeation Studies Of Nateglinide Nlc Loaded Transdermal Patches

To Determine The Unknown Plasma Drug Concentration Of Nateglinide A Calibration Curve Was Designed By Using Different Concentration Of Nateglinide. The Linearity For Calibration Curve Was Determined By Plotting The Peak Area And Nominal Concentration Of Nateglinide. For Linearity Study Eight Different Concentration Of Nateglinide Were Analyzed (0.04, 0.08, 0.12, 0.16, 0.2, 0.24, 0.28, 0.32 Mg/Ml). The Peak Area Response Was Found To Be Linear Over The Concentration Range Studied. The Coefficient Of Correlation 'R2' Was Found To Be 0.998. The Hplc Method By Interpolation Technique Has Been Successfully Used To Determine The Pharmacokinetic Datas From Unknown Plasma Drug Concentration Followed By Single Dose Administration Of Nateglinide (Coreg), Nateglinide Nlc (N16) And Nateglinide Nlc Transdermal Patch (Nt4). There Was A Significant Difference With $P < 0.05$ Between The Pharmacokinetic Parameters Of Marketed Nateglinide, Nateglinide Nlc And Nateglinide Nlc Loaded Transdermal Patch With Tmax Of 4hrs, 8hrs And 8hrs; Maximum Peak Plasma Concentration (Cmax) Of 0.258 Mg/Ml,0.208 Mg/Ml And 0.108 Mg/Ml Respectively. Area Under Curve (Auc0-A) Was Found To Be 125.127 Mg/Ml/H, 132.576 Mg/Ml.H, 841.032 Mg/Ml.H, Mean Residence Time Of Drug Mrt0- A Was Found To Be 17hrs, 19hrs And 82hrs Respectively. From The In-Vivo Pharmacokinetic Data It Was Concluded That Increase In Auc0-∞, Tmax, Mrt With Decrease In Cmax In Nlc And Nlc Loaded Transdermal Formulation When Compared To Marketed Available Coreg Cr Capsules.[15] On Calculating The Relative Bioavailability By Keeping Marketed Formulation As Standard, It Has Been Confirmed That Nlc Loaded Transdermal Patch Shows Enhancement Of Bioavailability Of About 6.72 % Than Other Two Formulations.

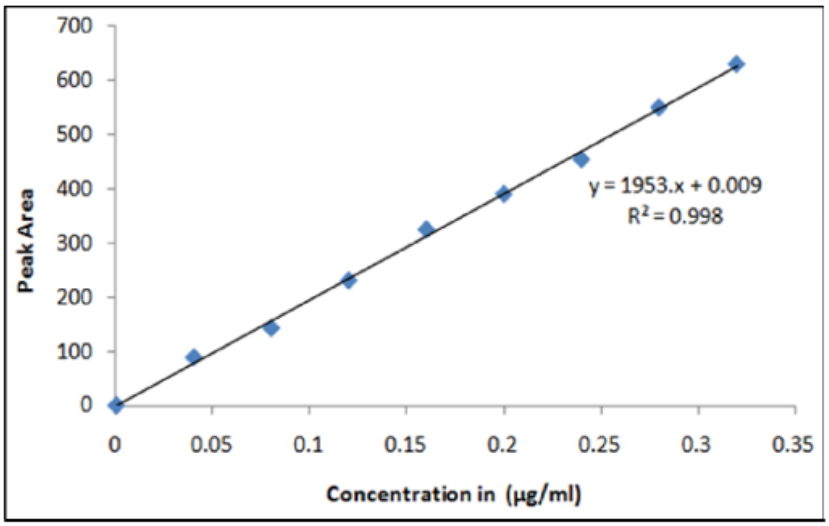


Figure 4 Calibration Curve For Nateglinide Pure Drug (Hplc)

The Effect Of Coreg Cr; Nateglinide Nlc (N16) And Nateglinide Nlc Loaded Transdermal Patch (Nt4) On Blood Sugar (Bs) Was Shown In Table 5.16 And Figure 5.129. During Induction Period Of Diabetes By High Sugar Diet The Negative Control Group Showed A Significant Increase (P<0.05) In Bs Of About 176.83±0.98mmhg, When Compared To Normotensive Control Groups 121.16±1.32 Mmhg.[16] After 14 Days Of Treatment, All The Treatment Groups Showed A Significant (P<0.05) Decrease In Bs Of About,126 .33± 0.52 Mmhg For 8hrs By Coreg Cr-G3; 121.33±0.52 Mmhg For 24 Hrs By Nateglinide Nlc-G4 And 121.5±0.54 Mmhg For 48 Hrs By Nateglinide Nlc Loaded Transdermal Patch-G5, When Compared With Negative Control Group. Based Upon The Results Obtained It Was Confirmed That Nateglinide Nlc Loaded Transdermal Patch Can Control Diabetes For A Prolonged Period Of Time I.E. For 48 Hrs.

Table 1 Effect Of Nateglinide Formulations On Blood Sugar Against Sugar Induced Diabetes In Rats

Experimental Group	**Blood Sugar (Mmhg In Hrs)***						
	0	**4**	**8**	**12**	**24**	**36**	**48**
G1 Control	121 ± 0.89	121.16 ± 1.32	121.5±1.76	121.5 ± 1.76	121.33± 1.50	121.16± 1.47	121.16± 1.32
G2 Negative Control	129.66 ± 0.82 *** (A)	136.66 ± 0.82 *** (A)	138 .66± 0.81 *** (A)	145.66± 0.82 *** (A)	147.5 ± 0.55 *** (A)	160.33 ± 0.51 *** (A)	176 .83± 0.98 *** (A)
G3 Positive Control	128.83 ± 1.16	123.33 ± 0.52 *** (C)	126 .33± 0.52 *** (C)	144.5 ± 1.22	146.33 ± 0.52	159.66± 1.50	175.83 ± 0.75
G4 Test 1	128.66 ± 0.82	135.66 ± 0.51 *(B)	121.5 ± 0.54 *** (C)	120.5 ± 0.54 *** (C)	121.33 ± 0.52 *** (C)	124.66± 0.51	173.5± 1.76
G5 Test 2	128.83 ± 0.75	135.16 ± 0.98 * (B)	121.5 ± 0.54 ** (C)	122 .16± 0.75 *** (C)	121.16 ± 0.42 *** (C)	123.5 ± 0.55 *** (C)	121.5± 0.54 *** (C)

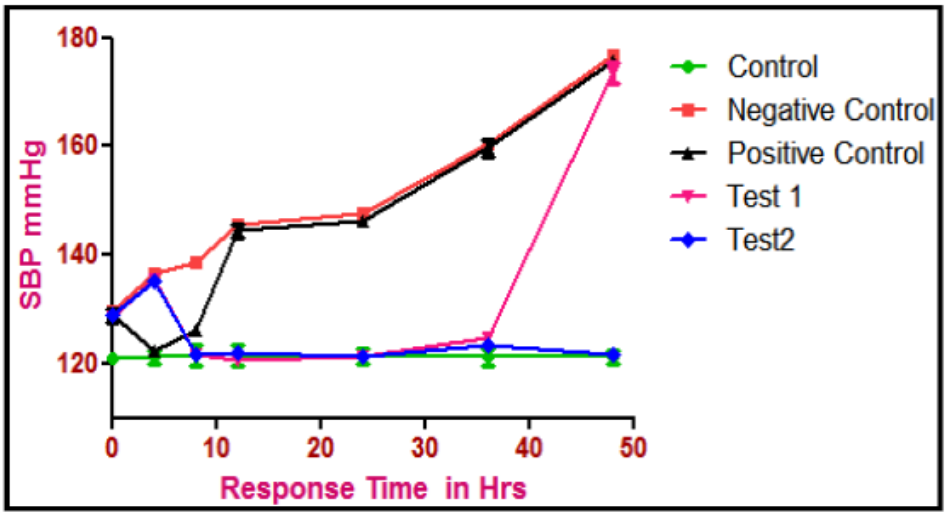


Figure Error! No text of specified style in document. **Effect Of Nateglinide Formulations On Blood Sugar Against Sugar Induced Diabetes In Rats (N=6)**

5. CONCLUSION

The Aim Has Been To Developed Therapeutic Nanotechnology Undertaking, Particularly For Targetted Drug Therapy The Smart Nlcs As The New Generation Offer Much More Flexibility In Drug Loading, Modulation Of Release And Improved Performance In Producing Final Dosage Forms The Objective Of This Research Is To Enhance The Bioavailability For Low Soluble (Bcs Class Ii) Drugs Such As Nateglinide In The Form Of Nlc Loaded Transdermal Patches. The Nlc Was Formulated And Optimized By The Parameters Like Particle Size (Ps In Nm), Polydispersity Index (Pi), Zeta Potential (Zp In Mv), % Drug Content, % Entrapment Efficiency And In-Vitro Drug Release For 24 Hrs Were Evaluated. The Best Optimized Nlcs Were Selected And Formulated Into Transdermal Patches. From This, It Was Concluded That Drug Loaded Nlc Transdermal Patch Will Be A Promising Drug Delivery System For Low Soluble And Poorly Bioavailable Drugs. The Nlcs As The New Generation Offer Much More Flexibility In Drug Loading, Modulation Of Release And Improved Performance In Producing Final Dosage Forms Such As Creams, Tablets, Capsules And Injectables. The Effort To Develop Alternative Routes And To Treat Other Diseases With Nlcs Should Be Continued To Extend Their Applications. As These Delivery Systems Can Be Easily Scaled Up For Large Scale Manufacturing, Hence Has A Lot Of Potential In The Forth Coming Years In The Pharmaceutical Field.

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