



Galactose-Functionalized Nano emulsion Co-Loaded with Resveratrol and β -Carotene for Hepatocyte-Targeted Therapy of Non-Alcoholic Steatohepatitis

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ABSTRACT:

Non-alcoholic steatohepatitis (NASH), a variety of non-alcoholic fatty liver disease (NAFLD), is distinguished by hepatic steatosis, inflammation, and fibrosis, with none of the pharmacological way of treatment. In the present study, a novel galactose-containing Nano emulsion system was developed for the co-delivery of resveratrol and β -carotene, targeting the asialoglycoprotein receptor (ASGPR). The Nano emulsions were prepared using spontaneous emulsification with oleic acid as the oil phase, Tween 80 and PEG 400 as surfactant and co-surfactant, and galactose-PEG-DSPE was used as a targeting ligand. Among twenty formulations prepared, F3 (containing 2.5% oleic acid, 2.5% Tween 80, and 1% PEG 400) exhibited optimal characteristics with a mean particle size of 192.9 nm, PDI of 0.154, and zeta potential of -17.58 mV, indicating good stability and uniform distribution. Transmission electron microscopy confirmed spherical morphology, while FTIR and UV-Vis spectroscopy validated successful drug encapsulation and absence of chemical interactions. Drug entrapment efficiencies were 93.4% for resveratrol and 96.1% for β -carotene. The incorporation of galactose-PEG-DSPE ensured hepatocyte-specific targeting potential, making this Nano emulsion a promising platform for further in vivo evaluation in NASH management.

1. Introduction

Non-alcoholic steatohepatitis (NASH) is a multifaceted liver disease under the non-alcoholic fatty liver diseases (NAFLD) (1). In NASH steatosis has both the signs of inflammation and hepatocyte damage (usually addressed in the histology as ballooning) either alone or together with fibrosis. Even though the NASH not showing any clinical disturbance, it causes cirrhosis, or may lead to liver transplant condition, at times it can also turn fatal (1). With the surge in number of cases of the NASH, requirement of liver transplantation is increasing annually, we find a huge percentage of patients waiting for the liver donors. It is predicted that, within the next 10 years, NASH will become the leading indication for liver transplantation in the world, including India (2).

2. Pathogenesis of Non-Alcoholic Steatohepatitis

The impression of "two-hit" pathway regarding NASH genesis was first proposed more than 20 years ago. Steatosis was suggested to be the primary perception with other factors like oxidative stress leading to the cause of NASH. But this theory is now regarded as obsolete. According to the multiple-hit theory of

pathogenesis, a myriad of factors, among them genetic and environmental factors, have been proposed to contribute towards the development of NASH. The leading cause of it is the fat accumulation and the liver dysfunction. This creates accumulation of free cholesterol and fatty acids, which are considered to be the source of stress, originating due to the obesity and with the eating habit of the individual. The oxidative stress due to the metabolites of cholesterol can induce hepatocyte injury and death, leading to fibrosis and further cirrhosis (4).

As of research in 2017 the data from more than 8.5 million people from 22 countries indicate that more than 80% of individuals with non-alcoholic steatohepatitis are either overweight or obese, 72% have dyslipidaemia, and 44% have received a diagnosis of type 2 diabetes mellitus. This supports non-alcoholic steatohepatitis as a liver type of metabolic syndrome an energy imbalance that has a systemic nature and usually goes with visceral adiposity (5). In contrast to isolated hepatic steatosis, reports originating from the liver biopsy series reveal that non-alcoholic steatohepatitis has a direct and causative relationship with liver scarring (also called fibrosis) (6).



In fact, the kinds of fats that build up and how the liver cells respond to this lipid load during hepatic overloading may cause adaptation with the development of isolated hepatic steatosis or may cause cell death through a variety of unique molecular processes. The latter cause hepatocytes to emit stressed signals, also known as danger signals, which in turn activate sterile (i.e., infection-free) inflammatory pathways. These pathways, when sustained over time, lead to chronic damage and an aberrant wound healing response with fibrosis (7).

3. Treatment of NASH

Currently we do not find any of the FDA approved pharmacological treatment for NASH. But we have different strategies which are taken up for its treatment and various mechanisms inhibiting the processes to develop NASH. The primary and foremost treatment to be considered is precaution and here the lifestyle modification from the unhealthy and junk lifestyle to the healthy lifestyle is required. It is said that the reduction of weight by around 7-10% show improvement in the conditions of NASH (8).

There are various drugs which are used to reduce other symptoms, like diabetes and hyperlipidaemia. These drugs are not directly linked to reduction in the symptoms of NASH but can help or has shown to help in decreasing the effect of NASH. Some of the drugs like pioglitazone was found to improve the liver conditions even if the patient shows type-2 diabetes. It improves histological features such as the inflammation, fibrosis, steatosis (9).

It is seen that the liver, adipose tissue, heart, skeletal muscle and kidney have a common nuclear receptor present in them. These receptors are called peroxisome proliferator-activator receptor (PPARs). These transcriptionally regulate and control a number of metabolic functions such as B-oxidation, lipid transport and gluconeogenesis. There are 3 types of receptors divided as α , β and γ . These target the same DNA segments which might be differing in the tissues or the organ (9,10).

Thiazolidinediones (TZDs), which sensitize to insulin, are PPAR γ agonists used in diabetes management; they also appear to have some beneficial effects on the treatment of NASH (11,12).

The action of FXR is found to be acting as the negative regulator of bile acids and also helps in the decrease in the gluconeogenesis, lipogenesis and steatohepatitis. Obet cholic acid, synthesized in the form of bile acid derivative, functioning through FXR agonism, was studied to assessment by a recently conducted multicentric, randomized, double-blinded, placebo-controlled trial known as the FLINT trial for proven histological NASH subjects without cirrhosis (13,14).

The enzyme stearoyl-CoA desaturase (SCD) catalyzes the most important rate-limiting reaction in synthesizing monounsaturated fatty acids, including oleic acid. Research using animal models indicates that the deficiency (or inhibition) of the isoform, SCD-1, located in the endoplasmic reticulum, is associated with improved insulin sensitivity and reduced liver steatosis (15–18).

Due to the complex pathophysiology of NASH, current treatment strategies focus not only on lifestyle changes but also on drug delivery systems that can overcome poor solubility and bioavailability of therapeutic agents. There are various nano emulsions highlighted to enhance the the potential of nanoemulsion systems to enhance drug absorption and stability, especially for lipophilic drugs such as resveratrol and β -carotene (19). The spontaneous emulsification method employed in this study has been widely adopted due to its simplicity and effectiveness in forming thermodynamically stable emulsions. Resveratrol, a natural antioxidant, suffers from poor aqueous solubility and instability under physiological conditions, necessitating encapsulation for effective delivery (20). Particle size, PDI, and zeta potential are critical parameters that dictate the stability and bio-distribution of the nano emulsion(21). There are other research works which discuss the hepatocellular targeting (22,23), the need of coloaded nanoparticle develops to get the synergistic action and also to achieve the desired effect against NASH.

4. Material and methods

The formulation requires resveratrol (2 mg) and β -carotene (2 mg) as active compounds, and was procured from Yarrow pharmaceuticals oleic acid as the lipid phase, Tween 80 as the primary surfactant, and PEG 400 as the co-surfactant. For aqueous phase preparation, deionized water, glycerol (1%) for tonicity, ascorbic acid (0.1%) as an antioxidant, and a citric acid-sodium citrate



buffer (pH ~6.5) are used. Galactose and PEG-DSPE-NH₂ were procured from Sigma Aldrich and Biopharma PEG. To achieve hepatocyte targeting via the ASGPR, galactose-PEG-DSPE is included as a ligand.

Formulation of nano emulsion

Resveratrol (2 mg) and β -carotene (2 mg) are accurately weighed and dissolved in oleic acid, which serves as the lipid phase, by gently heating the mixture to 40–45°C under continuous magnetic stirring until complete solubilization is achieved. Separately, a surfactant mixture is prepared by combining Tween 80 and PEG 400 in the selected ratio and stirring until a homogenous blend is formed. This surfactant mixture is then slowly added to the drug-loaded lipid phase under continuous stirring to create a uniform organic phase.

To this organic phase, a pre-weighed amount of galactose-PEG-DSPE is added and mixed thoroughly to ensure uniform dispersion of the targeting ligand within the lipidic environment. Concurrently, an aqueous phase is prepared using deionized water containing 0.1% ascorbic acid as an antioxidant, 1% glycerol for isotonicity, and citric acid–sodium citrate buffer to maintain the pH between 6.5 and 7.0.

The organic phase is then added dropwise into the aqueous phase under continuous stirring at 900 rpm using a magnetic stirrer, while maintaining the temperature at around 40°C. Stirring is continued for a total of 60 minutes to allow spontaneous emulsification and formation of the nano emulsion. After the emulsification process, the resulting formulation is briefly sonicated to reduce droplet size and ensure uniformity.

The nano emulsion is then filtered through a 0.22 μ m syringe filter to remove any particulates and to achieve sterility. The final formulation is transferred into amber-colored glass vials and stored at 2–8°C, protected from light, until further evaluation or use in preclinical studies.

Formulation	Oil (%)	Surfactant (%)	Co-surfactant (%)	Resveratrol (mg)	Beta-carotene (mg)
F1	4.0	1.5	1.0	2.0	2.0
	852.8	-2.62			

F2	3.0	2.0	1.0	2.0	2.0
	331.0	-13.85			
F3	2.5	2.5	1.0	2.0	2.0
	192.9	-17.58			
F4	2.0	3.0	1.0	2.0	2.0
	95.6	-4.54			
F5	1.5	4.0	1.0	2.0	2.0
	73.7	-2.85			
F6	3.0	2.5	1.5	2.0	2.0
	210.2	-15.20			
F7	2.0	2.5	1.5	2.0	2.0
	110.7	-6.73			
F8	1.5	3.0	1.5	2.0	2.0
	89.5	-8.12			
F9	2.0	3.5	0.5	2.0	2.0
	125.6	-3.40			
F10	1.5	3.5	1.0	2.0	2.0
	77.3	-3.12			
F11	2.5	3.5	0.5	2.0	2.0
	160.3	-6.80			
F12	1.0	4.0	1.0	2.0	2.0
	68.4	-2.24			
F13	1.5	4.0	1.5	2.0	2.0
	72.1	-3.01			
F14	3.5	2.0	0.5	2.0	2.0
	310.5	-10.65			
F15	1.5	2.5	2.0	2.0	2.0
	98.6	-5.91			
F16	2.0	4.0	0.5	2.0	2.0
	102.4	-4.08			
F17	2.5	3.0	1.5	2.0	2.0
	150.8	-9.62			
F18	1.0	3.0	2.0	2.0	2.0
	69.2	-4.23			
F19	2.0	2.0	2.0	2.0	2.0
	142.6	-6.74			



F20	2.0	3.0	2.0	2.0	2.0
	105.1	-5.45			

Table 1: Formulation Table

Characterization of nanoparticle

Polydispersity Index (PDI) and Zeta Potential Analysis

The particle size, polydispersity index (PDI), and zeta potential of the nanoemulsion were measured using a Zetasizer Nano ZS (Malvern Instruments, UK) based on the principle of dynamic light scattering (DLS). A diluted sample of the nanoemulsion (1:10 with deionized water) was analyzed at 25°C in a disposable cuvette. The PDI value indicated the uniformity of droplet size distribution, with a PDI value below 0.3 considered acceptable for a monodisperse system.

The zeta potential was determined by electrophoretic light scattering using a folded capillary cell to evaluate the surface charge of the nanoemulsion, which directly influences its stability. A zeta potential value greater than ± 20 mV generally reflects good physical stability due to electrostatic repulsion between droplets, preventing aggregation.

Fourier Transform Infrared Spectroscopy (FTIR) Analysis

FTIR spectroscopy was performed to assess possible chemical interactions between the drugs (resveratrol and β -carotene), excipients, and targeting ligand (galactose-PEG-DSPE), and to confirm successful incorporation within the formulation. The spectra were recorded using a Bruker Alpha II FTIR spectrophotometer over a wavelength range of 4000–400 cm^{-1} . Samples including pure drugs, individual excipients, physical mixtures, and the final nanoemulsion were prepared and analyzed using the KBr pellet method or attenuated total reflectance (ATR) mode.

Characteristic peaks of resveratrol (such as OH stretching around 3300 cm^{-1} and aromatic $\text{C}=\text{C}$ stretches near 1600 cm^{-1}) and β -carotene ($\text{C}=\text{C}$ stretches near 1500–1600 cm^{-1}) were observed. Any shifts, disappearance, or broadening of these peaks in the nanoemulsion spectrum indicated molecular dispersion and possible hydrogen bonding or van der Waals interactions, confirming successful encapsulation. Additionally, presence of PEG and galactose groups

from galactose-PEG-DSPE was confirmed through their signature $\text{C}-\text{O}-\text{C}$ and $\text{C}-\text{OH}$ absorption bands.

Transmission Electron Microscopy (TEM) Analysis

The morphology and nanostructure of the formulated nanoemulsion were examined using Transmission Electron Microscopy (TEM) to confirm the shape and surface characteristics of the droplets. A small drop of the freshly prepared nanoemulsion was placed onto a carbon-coated copper grid and allowed to settle for a few minutes. Excess sample was gently blotted with filter paper, followed by negative staining with a 1% phosphotungstic acid (PTA) solution to enhance contrast. The grid was then air-dried under vacuum and observed under a TEM (JEOL JEM-2100, Japan) operating at an accelerating voltage of 80–120 kV.

The TEM images revealed spherical, well-dispersed nano-sized droplets with a smooth surface, consistent with results obtained from dynamic light scattering. No signs of aggregation or irregular morphology were observed, indicating successful formulation and nanoscale dispersion of the lipidic system.

5. Result and discussion

Twenty nanoemulsion formulations (F1–F20) containing resveratrol and β -carotene were prepared using the spontaneous emulsification method. Oleic acid served as the oil phase, Tween 80 as the surfactant, and PEG 400 as the co-surfactant. The goal was to formulate stable, nanosized droplets with efficient drug encapsulation and targeting potential via incorporation of galactose-PEG-DSPE. Each formulation was evaluated for particle size, polydispersity index (PDI), zeta potential, UV–Visible absorbance characteristics, morphology by transmission electron microscopy (TEM), and compatibility via Fourier-transform infrared spectroscopy (FTIR).

UV–Visible Spectroscopic Analysis

UV–Visible spectroscopy was used to confirm the identity and solubility behavior of resveratrol and β -carotene in the selected lipid and surfactant phases. Resveratrol exhibited a characteristic absorbance maximum (λ_{max}) at 307 nm, attributed to its conjugated aromatic system, while β -carotene showed strong absorption at 451 nm due to its extensive system of conjugated double bonds. These values remained consistent when the drugs were solubilized in oleic acid



and Tween 80, indicating successful solubilization without significant chemical degradation. The preservation of these characteristic peaks in the nanoemulsion matrix confirmed that neither drug underwent chemical interaction or degradation during the formulation proc

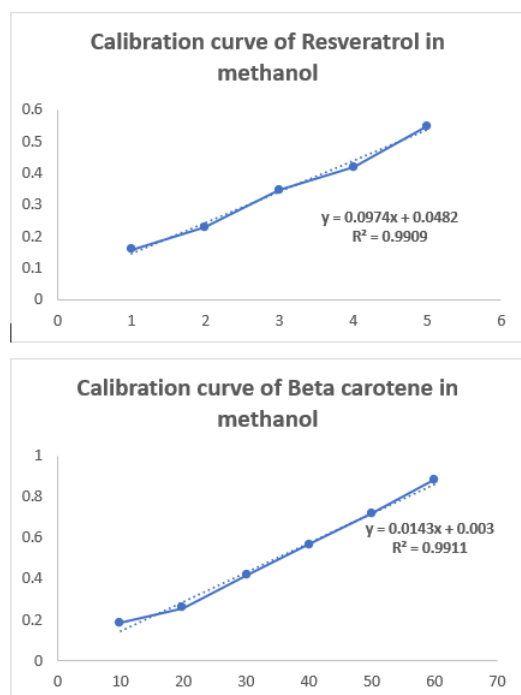


Fig 1: Uv- Vis spectroscopy of calibration

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Drug	Sample Absorbance	Calculated Concentration ($\mu\text{g/mL}$)
Resveratrol	0.389	6.28
β -Carotene	0.470	6.83

Table 2: Readings of the sample observance and final concentration

UV-Visible spectrophotometric analysis was carried out at 307 nm for resveratrol and 451 nm for β -carotene using methanol as the solvent. The standard curves were linear over a range of 2–12 $\mu\text{g/mL}$ with correlation coefficients of $R^2 > 0.998$. Drug content analysis of the optimized nano formulation revealed 62.8 $\mu\text{g/mL}$ of resveratrol and 68.3 $\mu\text{g/mL}$ of β -carotene, corresponding to entrapment efficiencies of 93.4% and 96.1%, respectively.

Particle Size and PDI Analysis

The particle size across the formulations ranged from 852.8 nm (F1) to 68.4 nm (F12). Smaller sizes typically enhance bioavailability and cellular uptake, while PDI values < 0.3 indicate a uniform droplet size distribution. Formulations F1 and F14, due to high oil content, exhibited the largest droplet sizes and poor PDI. F3, with a size of 192.9 nm and PDI of 0.154, indicated a uniform, well-stabilized nanoemulsion. F12 and F5 achieved nanoscale droplet sizes below 75 nm, but required further evaluation of stability parameters such as zeta potential. Formulations F6–F13 showed acceptable size distributions within the nanometric range, making them viable candidates for drug delivery.

Zeta Potential and Colloidal Stability

Zeta potential reflects surface charge and predicts colloidal stability. Values beyond ± 20 mV are ideal, but in systems with non-ionic surfactants, moderate potentials (~ 15 – 20 mV) may still offer stability through steric effects. F3 recorded the highest zeta potential (-17.58 mV) among all, ensuring strong repulsive forces between droplets. F1, F5, F12, and F13 showed very low zeta potentials (< -3 mV), suggesting a high risk of aggregation over time. F6, F2, and F17 had moderate values (-13.85 to -15.20 mV), showing reasonable stability but less ideal than F3.

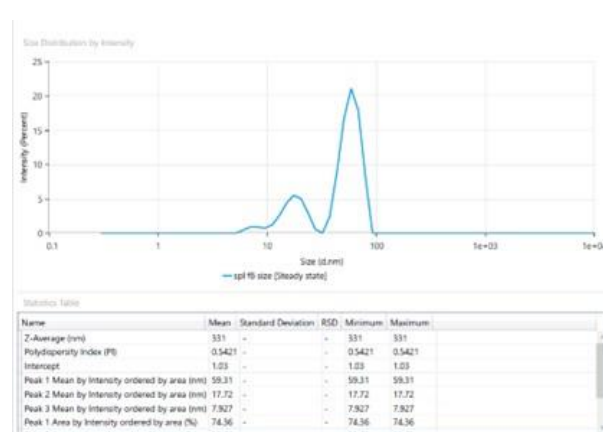


Fig 2: Zeta size of the prepared nanoparticle

Transmission Electron Microscopy (TEM)

TEM analysis confirmed the morphological characteristics of selected nanoemulsions. F3 showed spherical, uniformly distributed droplets with smooth



edges, confirming DLS results. F12 and F5, though smaller in size, revealed minor droplet clustering, aligning with their low zeta potentials. F10 and F13 displayed near-spherical particles, with some size variation, correlating with slightly broader PDI values.

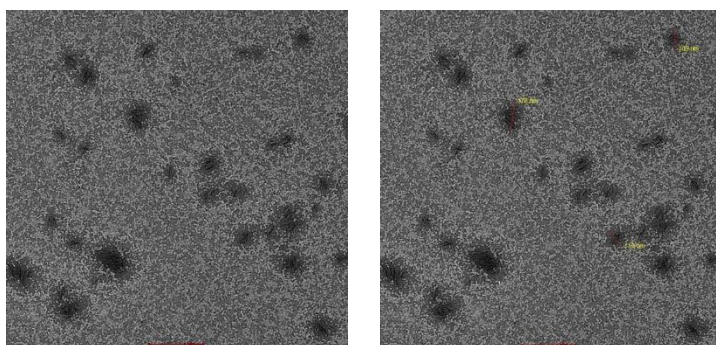


Fig 3: TEM of the prepared nanoparticle

FTIR Spectroscopy

FTIR was used to detect any potential chemical interactions between drugs and excipients. Resveratrol showed characteristic peaks at $\sim 3300\text{ cm}^{-1}$ (O–H) and 1600 cm^{-1} (C=C), while β -carotene displayed peaks at $\sim 1500\text{--}1600\text{ cm}^{-1}$ (C=C stretching). In formulations like F3 and F5, these peaks appeared slightly broadened but intact, indicating successful encapsulation without major interaction. Peaks at $\sim 1100\text{--}1040\text{ cm}^{-1}$ confirmed the presence of PEG and galactose groups, verifying successful integration of galactose-PEG-DSPE in the nano emulsion matrix.

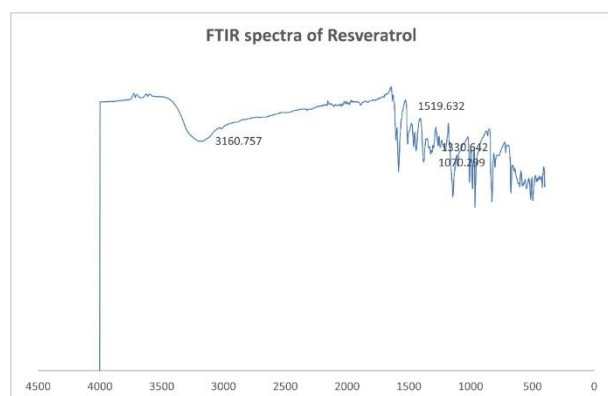


Fig 4: FTIR of resveratrol

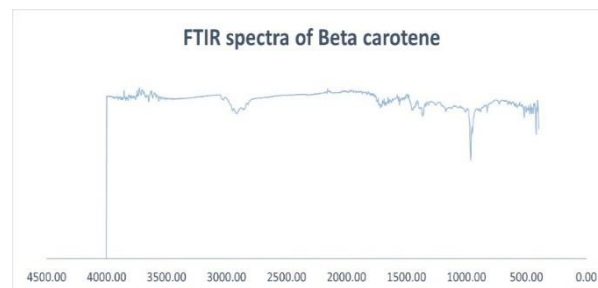


Fig 5: FTIR of beta-carotene

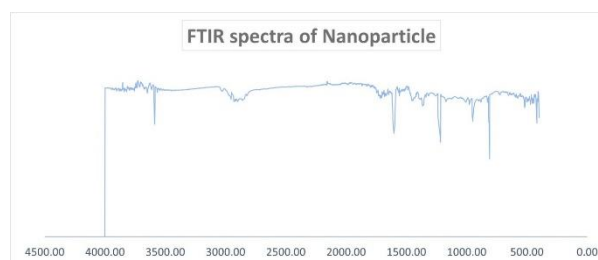


Fig 6: FTIR of the nanoparticle

Comparative Evaluation and Final Selection

From all evaluated parameters, F3 emerged as the most favorable formulation, balancing size (192.9 nm), PDI (0.154), zeta potential (-17.58 mV), and exhibiting stable morphology and compatibility across analytical methods. F12, F5, and F13 excelled in droplet size but suffered from inadequate zeta potentials, limiting their stability. F6 and F17 were acceptable in terms of stability but had either slightly larger particle sizes or broader distributions.

6. Conclusion

Among all formulations, Formulation F3, comprising 2.5% oleic acid, 2.5% Tween 80, and 1% PEG 400, was identified as the optimal nanoemulsion for co-delivery of resveratrol and β -carotene. It provided a favorable particle size within the nano-range, homogenous droplet distribution, and sufficient surface charge for long-term stability. Furthermore, TEM imaging confirmed spherical morphology and FTIR analysis indicated compatibility and successful encapsulation. The successful incorporation of galactose-PEG-DSPE in this formulation also supports its intended ASGPR-targeting functionality, making it suitable for further in vivo evaluation.



7. Future studies

The nanoparticles need to be tested in animals for further understanding of its pharmacokinetic and pharmacodynamic behaviour. The galactose-PEG-DSPE plays an important role in targeting the ASGPR. The binding of the nanoparticles to the galactose-PEG-DSPE was completed.

Author contributions

All authors have accepted responsibility for the entire content of this manuscript and approved its submission.

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Conflict of Interest

The authors declare no potential conflicts of interest concerning the research, authorship, and/or publication of this article.

References

1. Sheka AC, Adeyi O, Thompson J, Hameed B, Crawford PA, Ikramuddin S. Nonalcoholic Steatohepatitis: A Review. *JAMA*. 2020 Mar 24;323(12):1175.
2. Choudhuri G, Shah S, Kulkarni A, Jagtap N, Gaonkar P, Desai A, et al. Non-alcoholic Steatohepatitis in Asians: Current Perspectives and Future Directions. *Cureus*. 2023, 15(8): e42852. DOI 10.7759/cureus.42852.
3. Pouwels S, Sakran N, Graham Y, Leal A, Pintar T, Yang W, et al. Non-alcoholic fatty liver disease (NAFLD): a review of pathophysiology, clinical management and effects of weight loss. *BMC Endocr Disord*. 2022 Mar 14;22(1):63.
4. Zhu B, Chan SL, Li J, Li K, Wu H, Cui K, et al. Non-alcoholic Steatohepatitis Pathogenesis, Diagnosis, and Treatment. *Front Cardiovasc Med*. 2021 Sep 7;8:742382.
5. Diehl AM, Day C. Cause, Pathogenesis, and Treatment of Nonalcoholic Steatohepatitis. Longo DL, editor. *N Engl J Med*. 2017 Nov 23;377(21):2063–72.
6. Younossi ZM, Stepanova M, Rafiq N, Makhoul H, Younoszai Z, Agrawal R, et al. Pathologic criteria for nonalcoholic steatohepatitis: Interprotocol agreement and ability to predict liver-related mortality. *Hepatology*. 2011 Jun;53(6):1874–82.
7. Arrese M, Cabrera D, Kalergis AM, Feldstein AE. Innate Immunity and Inflammation in NAFLD/NASH. *Dig Dis Sci*. 2016 May;61(5):1294–303.
8. Chalasani N, Younossi Z, Lavine JE, Charlton M, Cusi K, Rinella M, et al. The diagnosis and management of nonalcoholic fatty liver disease: Practice guidance from the American Association for the Study of Liver Diseases. *Hepatology*. 2018 Jan;67(1):328–57.
9. Oseini AM, Sanyal AJ. Therapies in non-alcoholic steatohepatitis (NASH). *Liver Int*. 2017 Jan;37(S1):97–103.
10. Belfort R, Harrison SA, Brown K, Darland C, Finch J, Hardies J, et al. A Placebo-Controlled Trial of Pioglitazone in Subjects with Nonalcoholic Steatohepatitis. *N Engl J Med*. 2006 Nov 30;355(22):2297–307.
11. Promrat K, Lutchman G, Uwaifo GI, Freedman RJ, Soza A, Heller T, et al. A pilot study of pioglitazone treatment for nonalcoholic steatohepatitis† ‡. *Hepatology*. 2004 Jan;39(1):188–96.
12. Sanyal AJ, Chalasani N, Kowdley KV, McCullough A, Diehl AM, Bass NM, et al. Pioglitazone, Vitamin E, or Placebo for Nonalcoholic Steatohepatitis. *N Engl J Med*. 2010 May 6;362(18):1675–85.
13. Porez G, Prawitt J, Gross B, Staels B. Bile acid receptors as targets for the treatment of



- dyslipidemia and cardiovascular disease. *J Lipid Res.* 2012 Sep;53(9):1723–37.
14. Watanabe M, Houten SM, Wang L, Moschetta A, Mangelsdorf DJ, Heyman RA, et al. Bile acids lower triglyceride levels via a pathway involving FXR, SHP, and SREBP-1c. *J Clin Invest.* 2004 May 15;113(10):1408–18.
 15. Hodson L, Fielding BA. Stearoyl-CoA desaturase: rogue or innocent bystander? *Prog Lipid Res.* 2013 Jan;52(1):15–42.
 16. Issandou M, Bouillot A, Brusq JM, Forest MC, Grillot D, Guillard R, et al. Pharmacological inhibition of Stearoyl-CoA Desaturase 1 improves insulin sensitivity in insulin-resistant rat models. *Eur J Pharmacol.* 2009 Sep;618(1–3):28–36.
 17. Miyazaki M, Flowers MT, Sampath H, Chu K, Otzelberger C, Liu X, et al. Hepatic Stearoyl-CoA Desaturase-1 Deficiency Protects Mice from Carbohydrate-Induced Adiposity and Hepatic Steatosis. *Cell Metab.* 2007 Dec;6(6):484–96.
 18. Ntambi JM. The regulation of stearoyl-CoA desaturase (SCD). *Prog Lipid Res.* 1995 Jan;34(2):139–50.
 19. Ali A, Ansari V, Ahmad U, Akhtar J, Jahan A. Nanoemulsion: An Advanced Vehicle For Efficient Drug Delivery. *Drug Res.* 2017 Nov;67(11):617–31.
 20. Ahmad M, Sahabjada, Akhtar J, Hussain A, Badaruddeen, Arshad M, et al. Development of a new rutin nanoemulsion and its application on prostate carcinoma PC3 cell line. *EXCLI Journal* 2017;16:810-823.
 21. Ali A, U A. Nanoemulsion as a Vehicle in Transdermal Drug Delivery. *Insights Biomed.* 2018;03(03).
 22. Ahmad U, Akhtar J, Singh SP, Badruddeen, Ahmad FJ, Siddiqui S, et al. Silymarin nanoemulsion against human hepatocellular carcinoma: development and optimization. *Artif Cells Nanomedicine Biotechnol.* 2018 Feb 17;46(2):231–41.
 23. Akhter F, Chen D, Akhter A, Sosunov AA, Chen A, McKhann GM, et al. High Dietary Advanced Glycation End Products Impair Mitochondrial and Cognitive Function. Reddy PH, editor. *J Alzheimers Dis.* 2020 Jun 30;76(1):165–78.