Journal of Medical and oral biosciences
ISSN (Online): 3007-9551
ISSN (Print): 3007-9543

JMOB
Open Access DOAJ

IRAQI Academic Scientific Journals

Type: Review article
Publish online: 30/ 10/ 2025

Impact of Nanoliposomes on Hepatitis Virus Pathways: A narrative Review

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OPEN ACCESS

ARTICLE INFO
Received: 25/04/2025
Revised: 29 / 08/ 2025
Accepted: 18 / 10 / 2025
Publish online: 30/ 10 / 2025
Plagiarism percentages at publication: 17%

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CITATION

Bushra Shihab Hamad, Shahlaa Mahdi Shukr , Alaa Saadi Abbood (2025). Impact of Nanoliposomes on Hepatitis Virus Pathways: A narrative Review. JMOB. 2;(3): 55-65.
https://doi.org/10.58564/jmob.103

Abstract

Hepatitis viruses keep up to remain a significant worldwide health threat owing to their chronic nature, severe hepatic consequences, accompanied with the limited effectiveness of standard treatments. Nanoliposomes, which are lipid-based nanocarriers, have a lot of potential for improving the administration of antiviral drugs by making them more bioavailable, targeting the liver, and changing how the immune system works. This study intends to focus on the latest developments in the design, physicochemical properties, and processes of nanoliposomes that stop the hepatitis virus from spreading, with an emphasis on the hepatitis B and C viruses. Recent investigations demonstrate their capacity to improve antiviral drug stability, promote hepatic macrophage targeting, and impede viral multiplication, while diminishing systemic toxicity. Additionally, the research article addresses biocompatibility issues, the constraints of existing methodologies, and future prospects for the incorporation of nanoliposomes into combination therapies that include nucleoside analogues, immune-stimulants, and vaccines. Nanoliposome-based systems are a promising and potentially transformative approach for enhancing the therapeutic management of viral hepatitis.

Keywords: Hepatitis viruses, Hepatitis B virus, Hepatitis C virus (HCV), Nanoliposomes, Nanomedicine.

Introduction

Nano liposomes are essential in inhibiting pathways of hepatitis viruses, Nanoliposomes, functioning as phosphorus lipid carrier systems, can integrate with the natural outer membrane components of hepatitis viruses to produce diverse antiviral effects. Nanoliposomes may significantly influence hepatitis virus pathways by inhibiting viral replication, altering the host cell membrane, impeding initial infection stages, and enhancing the immune response, Currently, hepatitis virus infections constitute a significant global health concern (1). Nanoliposomes are Lipid nanoparticles are colloidal structures composed of lipid bilayers that encircle an aqueous nucleus. Nanoliposomes are typically 50–200 nm in size, with diameters spanning from 30 to 1000 nm. The distribution of phases as a function of composition is analogous to that of liposomes, and the phases exhibited by these systems are comparable (2). Nanoliposomes possess

significant potential for drug delivery, due to the fact that the bilayers can accommodate a diverse array of therapeutic molecules and the size-dependent dynamics enable the control of payload release from either the bilayer or the core (3).

Composition and mechanisms of action of Nanoliposomes

There are two ways that nanoliposomes can activate the hepatitis virus. The phospholipids of nanoliposomes combine with the viral phospholipid envelope, breaking it apart and stopping the virus from entering and reproducing. The nanoliposome core also releases polyphenolic compounds that stop the virus from replicating inside the host (4). nanoliposomes using phospholipids, cholesterol derivatives, steroids, surface-active compounds, and other carriers. Polyphenolic compounds that fight viruses, such as quercetin, rosmarinic acid, curcumin, and epigallocatechin gallate, can successfully combine with nanoliposomes. Adding cholesterol to the bilayer can make the treatment work better and make the membrane more stable (5). The lipid bilayer of nanoliposomes is usually made up of cholesterol, phospholipids, and glycerol. When mixed with cholesterol, the phospholipid DOPC (1,2-dioleoyl-sn-glycero-3-phosphocholine) can make a stable bilayer . This mix makes the membrane less fluid, which minimises the chance of overnight leakage (like curcumin), and when mixed with either polyethylene glycol or glycerol in the right amounts, it makes well-formed spherical vesicles. Cholesterol is an important part of the hepatitis B virus infection process and is found in the viral envelope. It affects replication and assembly. These results show that adding cholesterol to the nanoliposome bilayer is a beneficial way to stop viruses from working (6).

Mechanisms of Viral Inhibition by Nanoliposomes

There are many ways that nanoliposomes can stop viruses from spreading. Their major way of defending themselves is to use a protective barrier to catch pathogens. The features of the lipid bilayer enable nanoliposomes to interact with viruses, creating a protective barrier around their intended targets. Nanoliposomes are made from natural phospholipids. They are not very hazardous to cells and work well to stop the process of virus–host membrane fusion. Another way is that nanoliposomes affect the adsorption phase of the DENV reproduction cycle, which has a significant dose-dependent influence on the virus's ability to stop itself from spreading (7). This suggests that the virus's ability to bind to cell receptors is broken. Twelve nanoliposomes may stop the hepatitis virus from growing inside host cells (Figure. 1) when they are employed to treat the disease. Nanoliposomes make it easier for antiviral drugs to get into cells by fusing better with infected cells. Nanoliposomes improve drug stability and permeability by protecting encapsulated pharmaceutical molecules from breaking down in the gastrointestinal tract (8).

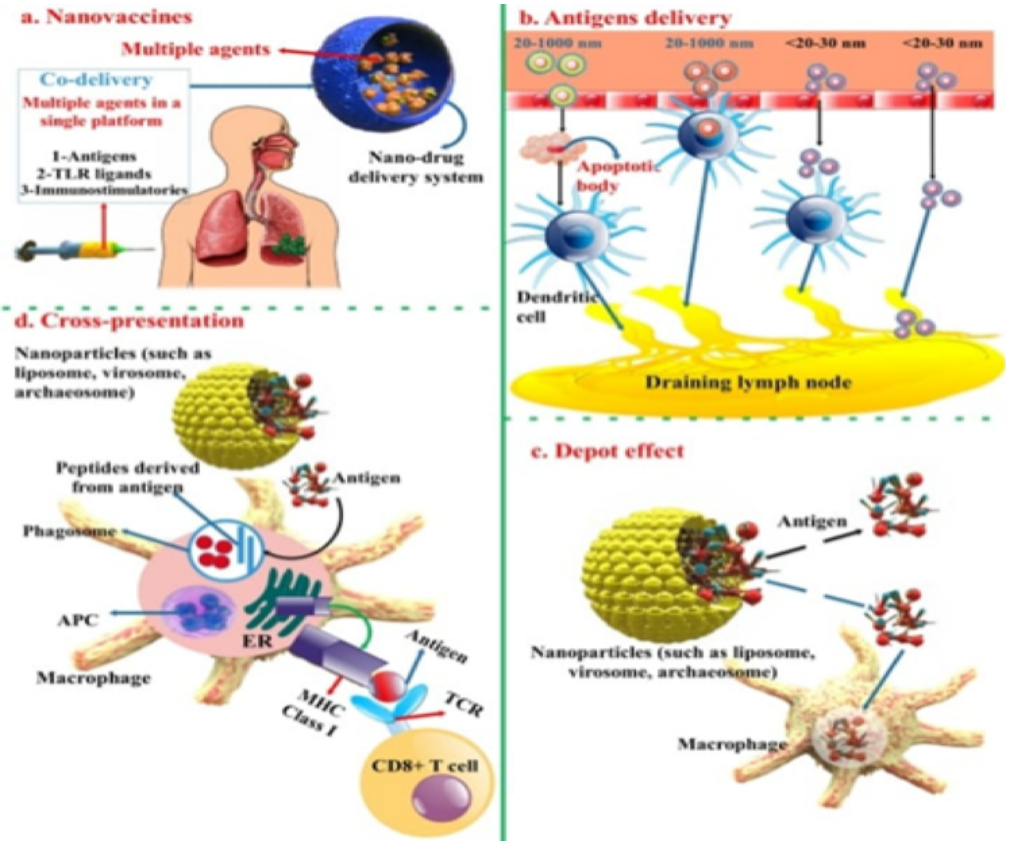

Figure. 1: Shows how nanoliposomes can help fight viruses by trapping them, stopping them from sticking to cells, delivering drugs by fusion, and controlling their release (9).

The history of nanoliposome research

The evolutionary advancement of nanoliposome research has undergone various phases The field has evolved from its initial emphasis on specialist-prepared therapy during the nucleic period to contemporary investigations into factors affecting hepatitis B virus HBsAg secretions. Seven additional subjects emerged; however, hepatitis research was not included in the current analysis, either in compound studies or as a specific research focus from 2005 to 2019 (10).

Initial Research on Nanoliposomes

Nanoliposomes were rapidly used as research instruments to investigate the determinants affecting the ingress of hepatitis viruses and their ensuing impacts on cells and tissues , Hepatic macrophages are essential in inhibiting the advancement of viral hepatitis. Nanotherapeutic strategies aimed at these cells entail the engineering of nanocarriers with tailored dimensions and surface alterations to facilitate both passive and active hepatic targeting (11). Infection with the hepatitis B virus (HBV) is still one of the top causes of death around the world. Current antiviral treatments sometimes don't eradicate the virus and usually need to be taken for a long time, which raises the risk of drug resistance. Researchers contend that forthcoming HBV treatment ought to integrate nucleoside analogues, immunostimulants, and vaccinations (12). Entecavir (E) is often recommended because it has been used in clinical settings for a long time, is quite

effective against viruses, doesn't cause much resistance to treatment, and is not very toxic. Recent cohort research indicated that E monotherapy was superior in suppressing HBV-DNA than combo treatments. Nonetheless, patient non-compliance and significant side effects linked to oral administration of E underscore the necessity for sustained-release formulations (13). There are now many long-acting parenteral formulations of E, including liquid crystalline systems, lipidic prodrugs, albumin nanoparticles, and poly(lactic-co-glycollic acid) (PLGA) microspheres. To improve targeting in the liver, carriers that have been optimised with subcellular targeting moieties have been used. Polymeric nanoparticles and lipid-based nanocarriers, including liposomes, are significant instruments in this domain. Liposomes are biocompatible, easy to modify, and the only nanocarriers that have been approved for use in medicine and industry (14).

Development in Nanotechnology

The development of polymeric nanoparticles and lipid nanocarriers represents a significant leap in improving the efficacy of liver targeting. Polymeric nanoparticles are beneficial because they can hold drugs that don't mix with water, break down naturally, and stay stable. People like liposomes and other lipid nanocarriers because they are biocompatible and simple to change the surface of. Liposomes are the only nanocarriers made in factories that are now allowed to be used in medical settings (15).
Hepatitis is a significant public health issue due to the high incidence of chronic hepatitis infection and the severe hepatic consequences that often occur. The hepatic plasma barrier diminishes the therapeutic efficiency of conventional pharmaceutical treatments by obstructing adequate medication access to the hepatic parenchyma. It is important to have the right delivery mechanism that can accurately target hepatocytes without going through the plasma barrier (16). Nanotechnology has made medicine delivery and gene therapy much better, Nanomedicine has gotten a lot of attention from doctors because it can target specific locations, make drugs more soluble, and make them less harmful. New nanomedicine treatments for hepatitis include liposomes, micelles, nanospheres, and anti-HBsAg protein-fused nucleocapsids. There are other known ways to use nanotherapeutics that target liver macrophages (17). Nanocarriers need to have a specified size and have surfaces that have been changed to make it easier for both passive and aggressive liver targeting,see Table.1. Even though oral entecavir works, sustained-release forms are needed because of side effects and low patient compliance , Consequently, investigations have been conducted on long-acting parenteral formulations of entecavir, including liquid crystals, lipidic prodrugs, albumin nanoparticles, and PLGA microspheres (18) .

Nanoliposomes in drug delivery systems

Substances that can be used as carriers include medicines, polymers, proteins, lipids, and surfactants. Historically, it was believed that lipid-based carriers could help increase the oral bioavailability of treatments that aren't water-soluble (19). Liposomes and polymeric micelles, two types of lipid-based nanocarriers, got a lot of interest as possible drug delivery carriers since they are more biocompatible and less toxic. The most well-known delivery vehicles are nanoliposomes, which have a phospholipid bilayer around the therapeutic chemicals. The key difference between them and regular liposomes is that they are smaller, which gives them a massive interfacial surface that may easily adsorb and interact with medications or biological species (20). Nanoliposomes may be better than regular liposomal formulations because the latter have a smaller specific surface area

and don't traverse membranes and intracellular organelles as well. Liposomes, utilised for medical objectives, presently represent the only nanocarrier sanctioned for clinical applications and expanded for industrial manufacturing. Nanocarriers ought to possess specific dimensions and tailored, designed, and altered surfaces to enable both passive and active (cellular targeting) liver targeting (21).

Table. 1: Targeted Nanomaterials for Hepatic Drug Delivery Systems (17)

Target Points	Cell Type	Nanomaterials
VCAM-1	Microvascular endothelial cells	Dexamethasone loaded anti-VCAM-1 SAINT-O-Somes
GA-R	Hepatoma cells	GA and PNA-modified DOX-loaded liposomes (DOX-GA/PNA-Lips); Glycyrrhetinic acid-modified oxaliplatin liposome (GA-OX)
ASGPR	Hepatocytes	Galactose Modified Liposomes (Gal-LP); Celastrol-Loaded Galactosylated Liposomes (C-GPL); ASF-lipoplexes; Lactobionic acid coupled liposomes (LA-LP)
Folate receptor	Hepatoma cells	Folate-targeted curcumin-loaded chitosan-coated magnetic nanoparticles; Folate modified oxaliplatin liposome (FA-OX)
EGFR	Hepatocellular carcinoma	EGFR-targeted immunoliposomes
Transferrin receptor	Hepatocellular carcinoma	Transferrin-guided chitosan nanoparticles
Integrin αvβ3	Liver cancer cells	RGD modified liposome

Targeted Delivery Systems

Nanoliposome (NLP) delivery of the hepatitis virus directly targets vaccinations and medications to the virus's areas of action while also reducing the serum or local concern about vaccine or drug aggregation in the body (Figure. 2) , Choosing the size of the footprint lowers blood clearance and DNA-related damage. The HPV tumour surface is simultaneously exposed via a corona targetable location within the lipid shell for nucleic acids, while fully preserving the arginine-lipofurbing function of two Nano cimicifugoside Phasers (NLP-CG) ,The arginine NP-CG pathway, in particular, causes CD4-positive POS toxin, POS transfer factor, and lysis cytokines (iNOS, TNF-α), and related splenocytes to interfere with the human THP-1 MHMC/THPM interaction with transitional HPV tumour cells (22). HDL, LDL, globin, cytokines, activated T cells, rings, and weariness are in the antibody-coated liposome. Change liposome bait surface, concentration, or volume whenever you desire. HPV NA promotes HPV by activity BMPs that naturally kill HPV. This vaccination contains oocyte HPV and other sources. Nucleics. HPV nucleic acid vaccine (TUC) is another. Check figure. Rapid growth, stability, and lack of host genome integration make mRNA helpful in immunotherapy.

It's still a common flu vaccination failure and a terrible NAHI or RPMV mRNA-based vaccine. Additionally, researchers are studying it as a cancer treatment (23).

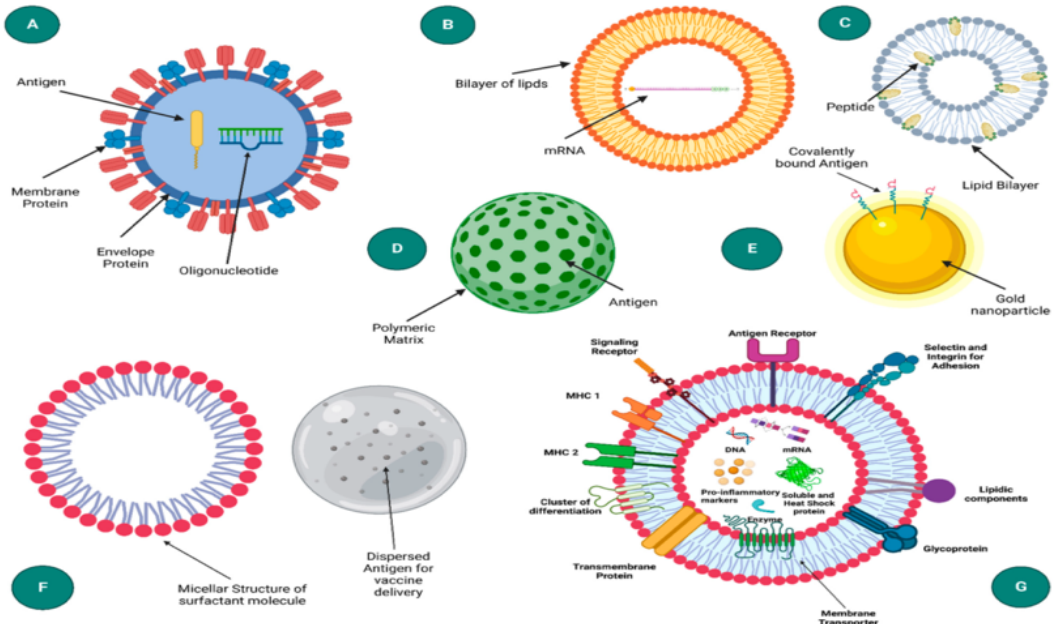

Figure. 2: Showing how different nanoparticle-based delivery systems work: (A) virus-like particle, (B) liposome, (C) ISCOM (immune-stimulating complexes), (D) polymeric nanoparticle, (E) inorganic nanoparticle, (F) emulsion, and (G) exosome (23).

Hepatitis Virus Overview

Hepatitis viruses are categorized into multiple genus groups with distinct pathogenesis patterns based on their structural and genomic characteristics:

- Hepacivirus
- Pegivirus,
- Pestivirus, which cause chronic hepatitis and fibrosing cholestatic changes and belong to the Flaviviridae family
- Teschovirus
- Tremovirus, both linked to unknown hepatitis
- Hepatovirus, which causes acute hepatitis and belongs to the Picornaviridae family
- Orthohepadnavirus, an enveloped DNA virus that causes chronic hepatitis and hepatitis D infection.

High-risk practices like blood transfusions, household item exchanges, unprotected sex, needlestick injuries, and vertical transmission are all ways that hepatitis viruses spread, Viral entry into target cells is facilitated by a variety of particular receptors and viral ligands during penetration (cell attachment) ,These mechanisms affect the spread of disease and infectivity, The number of infected cells is determined by the affinity between

the viral ligand and receptor, For example, the hepatitis B virus (HBV) first interacts with heparin sulphate proteoglycans (HSPGs) on the liver surface before entering hepatocytes It then attaches itself to the sodium taurocholate co-transporting polypeptide (NTCP), which is its secondary receptor (24). The pre-S1 domain of HBV's large hepatitis B surface antigen (LHBsAg) interacts with hepatocyte receptor binding sites, Pre-genomic and genomic RNA transcription, core and envelope protein synthesis and transport, nucleocapsid assembly, RNA packaging, reverse transcription, maturation, and release are all steps in virus replication. The viral nucleocapsid is where HBV DNA synthesis takes place (25). Mature nucleocapsids either join with envelope proteins to leave the cell or return to the nucleus to repair partly double-stranded DNA and encourage the production of cccDN as show in Figure. 3.

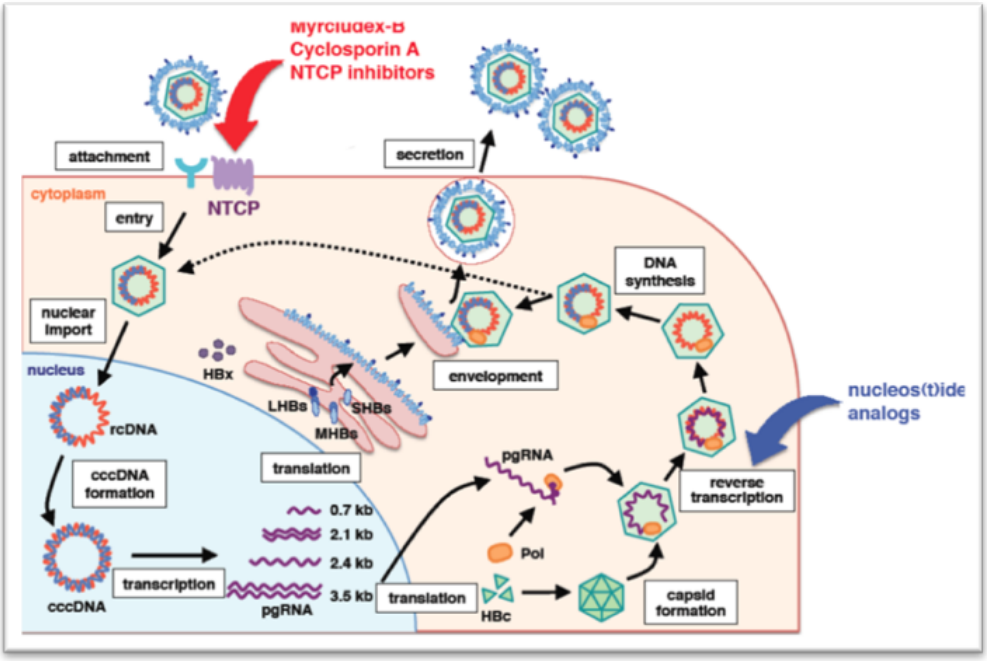

Figure. 3: Shows the HBV lifecycle and the way NTCP spreads the virus (26).

Hepatitis Virus Types

Researchers have thoroughly investigated the mechanisms underlying liver disorders induced by hepatitis viruses, particularly hepatocellular carcinoma. Successful intervention can take place in the early or late stages of hepatitis virus infection, regardless of therapy advancements (27) . According to published reports, the anti-HBV activity of a plant extract-loaded nanoliposome system made with methanol, methylene chloride, and ethyl acetate was examined, The lipid components were cholesterol and soybean phospholipids, and the final encapsulated extract made up 88.05% of the original powder,By modifying the ratios of ingredients and formulation elements, as well as by managing variables including material types, pH, temperature, and hydration stage time, a very high extract-loading efficiency was attained (28). However, studying viral metabolism and developing antiviral medicines like nanoparticles and nanosomic require a thorough understanding of viral infection mechanisms. Current cancer research focuses on immune cells and signs that slow cancer growth and aid healing. Five hepatitis viruses

exist: A, B, C, D, and E. Types B and C cause most long-term infections. There are various ways viral particles enter the body. A and E indicate food and drink contamination. The virus enters the bloodstream through the digestive system and enters the small intestine through the biliary tract, where it appears in feces. Sexual contact, blood exposure, and mother-to-child transmission can spread blood-borne hepatitis B, C, and D viruses. Once in the liver, the virus enters the circulation and is released in bile (29).

The Pathophysiology of Hepatitis

Hepatotropic viruses A, B, C, D, and E cause acute and chronic liver inflammation,Many term this "liver inflammation" or "hepatitis." Hepatitis A, B, C, D, and E prevalence varies worldwide. HDV infection ranges from 0.98% to 45% by location. Faecal–oral hepatitis viruses include HAV, HEV, and HGV (30). This is primarily due to poor handwashing. HEV is a Hepeviridae and Hepevirus genus. The Picornaviridae family and Hepatovirus genus include HAV. Twenty to twenty-five percent of pregnant HEV patients die. APASL (Figure. 4) states, "Acute liver failure is an acute liver disease associated with encephalopathy within 4 weeks of the onset of symptoms; it is a clinical entity with high morbidity and mortality and will lead to multiorgan failure and death or liver transplantation if not treated conservatively." The deadly condition acute liver failure (ALF) requires a liver transplant (30).

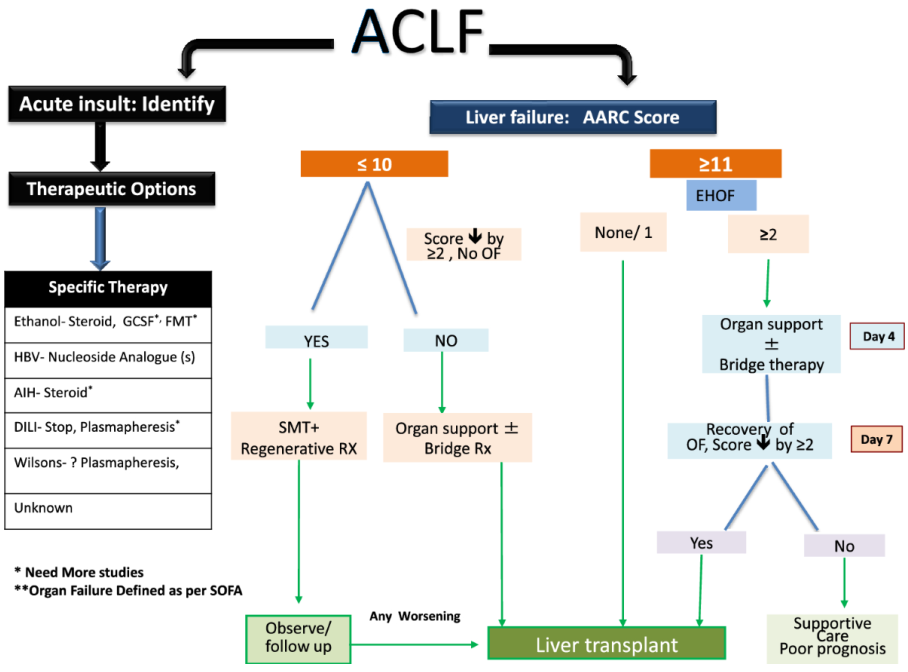

Figure. 4: Shows the APASL definition and pathophysiological process of ACLF in acute hepatic insult (30).

The Effect of Nanoliposomes on Hepatitis Virus Pathways

Nanotherapeutic targeting of hepatic macrophages is crucial for the prevention of viral hepatitis. To target the liver with nanocarrier delivery methods, you need to take exact

measurements and change the surface. The ineffectiveness of certain antivirals in eradicating the hepatitis B virus (HBV) raises concerns over treatment resistance and constitutes a significant cause of mortality associated with liver cancer and cirrhosis (31). Even though entecavir (E) was chosen because it is antiviral, moderately toxic, and has a low resistance profile, sustained-release versions of the drug were made because taking it by mouth is connected to poor patient compliance and adverse side effects. The study investigates various long-acting parenteral delivery methods, such as lipidic prodrugs, albumin nanoparticles, PLGA microspheres, and liquid crystals, focusing on carriers with targeting moieties to improve hepatic selectivity. Polymeric nanoparticles are more stable and can hold more drugs than liposomes and other lipid nanocarriers. Some liposome compositions have even been approved for use in medicine (32). Nanoliposomes that are loaded with drugs designed to lower or eliminate HBV represent a technique for targeting the liver while simultaneously providing medications for hepatic imaging. This approach makes it possible for future treatments that improve patients' quality of life by combining immune-stimulants, vaccines, and nucleotide analogues . For the creation of receptor-specific nanocarrier systems, a thorough understanding of liver cell receptors is necessary to improve therapeutic efficacy. The asialoglycoprotein receptor is a liver-specific receptor that researchers are currently studying. It helps the body take in galactose or N-acetylgalactosamine residue-containing moieties (33).

Effectiveness in Hepatitis Treatment

Hepatitis B virus (HBV) is a major global health issue because it can lead to liver disorders that Antiviral nucleoside analogues like entecavir (E) are still the best therapy for HBV since they are strong, don't cause much resistance, and don't cause much harm to the body. But right now, oral E is linked to bad side effects and patients not following through with their treatment. To solve these problems, parenteral long-acting formulations are being made. In this context, a rationally designed, sustained-release nanoplatform is described for the effective delivery of E in the treatment of HBV and related hepatic viral disorders (34).

Viral Replication Inhibition

Infected hepatocytes can be selectively delivered an appropriate antiviral compound by a nanocarrier, while healthy cells and tissues are spared from toxicity. Virion production and propagation are effectively inhibited by agents that interfere with hepatitis virus replication , a complex process that is controlled by cellular determinants (35). The host's lipid metabolism influences viral assembly, maturation, degradation, and secretion, while host processes such as geranylgeranylation and fatty acids regulate viral replication. In the late stages of viral infection, exogenous compounds with recognised broad-spectrum antiviral activity, such as Soraphen A (an acetyl CoA carboxylase inhibitor) (Figure. 5) , inhibit the replication and infectivity of enveloped viruses that utilise de novo-generated lipids and membrane-assembly platforms. Membrane lipids also influence virion behavior. Viral proteins interact with cellular organelles to alter the intracellular membrane lipid landscape, which in turn influences intracellular trafficking and the assembly site (36) .

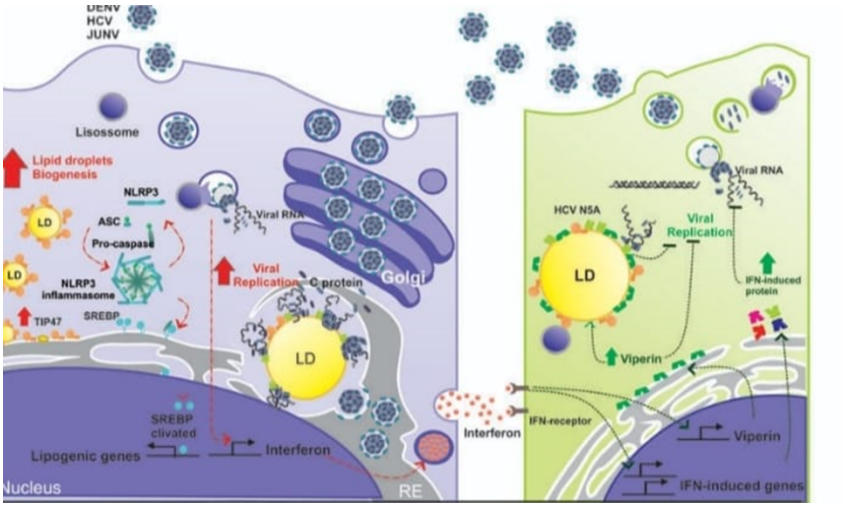

Figure. 5: Viral proteins, including HCV core and NS5A, are found in lipid droplets, which are near the ER and help the virus replicate. De novo lipogenesis (ACC/FAS-driven) provides the lipid scaffolds that are needed for virion assembly (37).

The Immune Response's Current State

Through regulation of inflammatory cytokine expression in relation to hepatitis viruses, nano-liposomes can improve antiviral effectiveness. To eradicate intracellular viral infections, the immune response must maintain a balance of inflammatory cytokines in viral hepatitis. As the severity of viral hepatitis increases, the cytokine profile shifts . Gamma interferon and tumour necrosis factor alpha are produced by cytotoxic T lymphocytes; these molecules inhibit viral replication and prevent enlargement of the liver (38). Several cytokines, including interleukins 6 and 10, are involved. A chronic HBV infection can develop when there is an imbalance in the expression of certain cytokines, which might hinder the body's inflammatory response and throw off immunological homeostasis. A stearylamine-conjugated immuno-liposome was created by M. G. Smits et al. to target antigen-presenting cells with the hepatitis B virus core viral epitope peptide 18-27 (HBcAg132-148aa). More major histocompatibility complex class I molecules were expressed in response to immunoliposomes (39). The production of more gamma interferon-cytokines by the antigen-specific T-cells contributed to the establishment of a type-1 cytokine environment. Immunoliposomes containing the viral core epitope peptide have the potential to be a therapeutic vaccination that protects the liver and promotes HBV clearance by CTL. Analysing Research Results Comparatively Systematic comparisons can enhance our understanding of the research trajectories related to nanoliposomes and hepatitis viruses. One potential strategy for HBV eradication is the use of immunomodulatory medications in conjunction with first-line antiviral nucleoside analogues like entecavir (40). A hepatotropic lipoplex system with 2'-O-methyl phosphorothioate-modified siRNAs successfully injects into the circulation to silence genes targeting the liver, and a coupled vitamin E-coated polymer hybrid nanoplatform enhances long-term macrophage retention. In vitro and in vivo, hepatocyte-targeted cargo distribution is facilitated by a synthetic HBV preS-derived lipopeptide (HBVP) attached to polyethyleneglycolylated liposomes (41). Models suggest that extending a chemically or recombinantly synthesised lysine-alanine oligopeptide brush on the liposome surface can enhance cellular absorption. Brushes with many (1–7) copies

of the -K–A–dipeptide and lysine at the end are better able to form electrostatic contacts with heparan sulphate proteoglycans, which are negatively charged. For the polymer brushes to keep their high HBV preS1 binding avidity, their average side length should be less than the typical liposome radius, which can range from 25 nm to 100 nm. According to a comparison simulation of many variations, these parameters improve the initial HBV-PreS1-HBVP binding process and make targeting more successful (42).
In addition, there are crucial processes that follow in producing HBVP-modified liposomes, controlling drug encapsulation and release studies, evaluating targeting properties in vitro, and evaluating the impacts of HBV replication inhibition in vivo (43).

Research Supporting the Effectiveness of Nanoliposomes

Despite efforts to eradicate it, hepatitis viruses, notably hepatitis B virus (HBV), continue to be a significant global public health issue. Nanotherapeutics are being researched as alternative therapies. Nanoliposomes are appealing candidate carriers due to their capacity to (i) (i) accumulate in the liver, (ii) encapsulate substantial quantities of diverse compounds, (iii) safeguard the compounds, and (iv) exhibit biocompatibility; they are also the sole class of nanocarrier sanctioned for clinical applications and scalability (44). PEGylated nanoliposomes are thought to enhance the systemic exposure of encapsulated compounds while reducing adverse reactions in comparison to oral treatment. Pluronic-stabilised nanoliposomes demonstrated efficacy as a carrier for extremely hydrophobic acyclic nucleoside phosphonate mimics, potentially influencing hepatitis C virus prevalence. A sequence of imidazo [4,5-b] PEGylated nanoliposomes appear to be an effective delivery system for enhancing both the solubility and antiviral efficacy of pyridine-5-carboxamide-substituted macrocyclic derivatives that are structurally related to acyclic nucleoside phosphonates. This is evidenced by encapsulation resulting in prolonged activity and diminished cytotoxicity against the replication of the hepatitis B virus (45).

Conflicting Results and Constraints

Nanoliposomes' effect on hepatitis viruses is unclear, Researchers believe nanoliposomes stimulate signaling pathways to promote viral RNA replication, However, other research suggest that nanoliposomes may inhibit viral protein interactions, stopping replication. More investigation is needed due to this disparity (46). Strategies for targeting hepatic macrophages with nanotherapeutics are well-defined. The nanocarriers' size and surface must be changed to facilitate passive and active liver targeting. Future HBV treatment should include nucleoside analogues, immunostimulants, and potentially curative vaccines. Its efficacy, low systemic toxicity, and little resistance make entecavir (E) highly recommended. However, oral administration has limited patient compliance and undesirable side effects, hence sustained-release formulations were developed (47). Long-acting parenteral forms of E like liquid crystals, lipidic prodrugs, albumin nanoparticles, and PLGA microspheres have been studied. Optimized carriers containing subcellular targeting moieties, such as polymeric nanoparticles and liposomes, increase hepatic targeting. Liposomes are interesting because they are safe and easy to change. They're the only nanocarriers approved for clinical and mass production. Nanocarrier systems with receptor-specific ligands may improve therapy. They could also deliver drugs and take liver images simultaneously. New therapy alternatives and drug carriers can still eliminate or dramatically reduce HBV, improving patients' lives (48).

Possibility of Combination Therapies

Nanotherapeutics delivery techniques offer pathways to specifically target hepatic macrophages, which are crucial in inhibiting disease development in viral hepatitis. Nanocarriers with precisely calibrated dimensions and efficient surface alterations can specifically target the liver, The present state of hepatitis B treatment is a combination of nucleoside analogues, immunostimulants, and potentially curative vaccinations. Entecavir (E) is a well-known nucleoside analogue because it is quite effective, has little resistance, and is not very harmful. Moreover, E monotherapy results in a more significant and prolonged suppression of HBV-DNA in comparison to combination therapies. Nonetheless, the parenteral route facilitates the development of long-acting formulations that address inadequate patient compliance and the challenges associated with oral administration (49). Liquid crystals, lipidic prodrugs, albumin nanoparticles, and PLGA microspheres provide these techniques. Subcellular targeting moieties on carriers improve the targeting of these systems to the liver. Polymeric nanoparticles have many good qualities, such as being able to hold many drugs, breaking down naturally, and being stable. Lipid nanocarriers, like liposomes, are still a very popular platform since they have a lot of clinical experience due to their biocompatibility and easy surface modification. Liposomes are the nanocarriers of choice for clinical approval and industrial manufacturing (50).

New ideas for designing Nanoliposomes

Nanoliposomes may be useful for treating various health issues by delivering drugs to the liver. Nanoparticles can also be used to help with diagnosis, mark specific liver parts, and improve contrast in imaging. Researchers have used both lipid and polymer platforms to make different nanoplatforms that work better in vivo to deliver anti-HBV medicines. Polymeric nanoparticles can hold drugs well, break down naturally, and be more stable (51). Lipid nanocarriers, such as liposomes and niosomes, are very biocompatible and easy to change. The pharmaceutical industry only allowed liposomal nanocarriers to start clinical production for parenteral distribution. A hybrid nanoplatform composed of vitamin E-coated vesicular polymer and docetaxel-loaded poly(d,l-lactide-co-glycolide) (PLGA) nanoparticles has been reported to exhibit prolonged release and improved in vitro macrophage retention, presenting a promising anti-hepatitis B treatment avenue. An advantageous trait of nanocarriers, enhancing anti-HBV therapy, is their ability to integrate agents alongside the necessary medication for liver imaging. The identification of new medication candidates and their corresponding carriers is expected to be advantageous in the eradication or substantial decrease of HBV. Future anti-HBV therapeutics are anticipated to integrate medicines like nucleoside analogues, immunostimulants, and vaccines. When these goals are met, the quality of life for patients will increase a lot (52).

Regulatory and Ethical Considerations

In the last decade, the significance of liver diseases, particularly their high mortality rates, has increased. HBV-related clinical symptoms such as cirrhosis, hepatocellular carcinoma, and liver failure remain the greatest health risk worldwide. Furthermore, the hepatitis B virus is able to induce both acute and chronic liver damage (53). Any hepatitis B therapeutic system could be considered effective if it is able to reach and maintain the

required drug levels within hepatic macrophages. In association with related antiviral agents and immunomodulatory molecules, the therapeutic platform is meant to serve as a stand-alone treatment for HBV. Hepatic macrophages play a pivotal role in preventing the progression of viral hepatitis. Consequently, various nanotherapeutic-delivery strategies have been prescribed for targeting hepatic macrophages. Since an effective HBV treatment is still not available, researchers have developed different anti-hepatitis-B drugs to manage the viral load. Furthermore, suitable nanodelivery systems are assumed to be a vital approach for developing prolonged- or targeted-delivery systems to infected areas . Accordingly, many polymeric and lipid bilayer-based nanocarriers that encapsulate such agents have been fabricated. These vehicles hold enormous promise for reducing and eventually eradicating the virus in the future (54). Although one nano- or microtechnique may show promise for a given antiviral agent, there is no stand-alone technique that effectively resolves all the issues and limitations encountered by current anti-HBV agents and treatment regimes. Receptor-specific ligands can thus be incorporated in the design of nanocarrier systems to achieve heightened efficiency of therapy and incorporate agents for liver imaging. Future anti-HBV therapies are expected to embrace a medley of agents, such as nucleot(s)ide analogues, immune-stimulants, and curative vaccines. Once these ideals have been reached and achieved, quality of life will be greatly improved for patients suffering from this debilitating disease (55).

The Safety Record of Nanoliposomes

It's important to be concerned about the possible toxicity of every new bioactive material because hazardous molecules might have long-term impacts even in little amounts. Therefore, it's very important to ensure that any new drug carrier is given as little as possible and stays in the body for a long time. Liposomes have been one of the most studied nanocarriers because they are biocompatible, easy to make, can target and change surfaces, can hold many drugs, and have been approved for commercial production. Liposomes make it possible for drugs to get into cells in several ways, such as by passively releasing them into the extracellular space, fusing with the plasma membrane, or endocytosis (56).

The Moral Effects of Nanotechnology

Using nanotechnology to make medications that fight hepatitis B involves serious moral issues that need to be thought about properly. Vitamin E-coated polymer hybrids and polymer-lipid nanoplatforms are two types of hepatic delivery nanocarriers that let imaging agents be added to them so that treatment may be tracked and drugs can stay in the target locations longer. However, there are still challenges to overcome, including the fact that viral loads cannot be eliminated and the risk of medicine resistance that occurs with long-term antiviral treatment. The intended method for the future, which entails mixing immune-stimulants, therapeutic vaccines, and nucleoside analogues, shows a way to be more thorough. A multi-pronged approach is needed, with nanotechnology playing a minor role (57, 58).

Conclusion

Nanotherapeutic methods targeting hepatic macrophages by passive and active liver targeting may help regulate vascular issues during hepatitis infection. Entecavir is safe

and effective, however it doesn't act well orally. This tendency has resulted to long-acting parenteral systems such lipidic prodrugs, albumin nanoparticles, and PLGA microspheres. Polymeric nanoparticles are good for drug stability and loading, but liposomes are superior for biocompatibility and surface flexibility. Liposomes are the only nanocarrier approved in clinical and industrial environments.

Declarations

Acknowledgment

The authors would like to thank Mustansiriyah university/ Baghdad/ Iraq for support in completing this research

Ethics statement

The authors confirm that this research complies with the journal's ethical approval requirements and has been prepared in accordance with the ethical guidelines stated on the journal's author guidelines page.

Funding

The authors stated that this work received no funding.

Competing interest's statement

The authors declare that they have no conflict of interest.

Author contributions

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References

1. Hamdi M, Abdel-Bar HM, Elmowafy E, Al-Jamal KT, Awad GAS. An integrated vitamin E-coated polymer hybrid nanoplatform: A lucrative option for an enhanced in vitro macrophage retention for an anti-hepatitis B therapeutic prospect. PLoS One. 2020 Jan 10;15(1):e0227231. doi: 10.1371/journal.pone.0227231.

2. Singh L, Indermun S, Govender M, Kumar P, du Toit LC, Choonara YE, Pillay V. Drug Delivery Strategies for Antivirals against Hepatitis B Virus. Viruses. 2018 May 17;10(5):267. doi: 10.3390/v10050267.

3. Tripathi SK, Li Y, Luo G. Syndecan 2 proteoglycan serves as a hepatitis B virus cell attachment receptor. J Virol. 2025 Jul 22;99(7):e0079625. doi: 10.1128/jvi.00796-25.

4. Shi Y, Du L, Lv D, Li Y, Zhang Z, Huang X, Tang H. Emerging role and therapeutic application of exosome in hepatitis virus infection and associated diseases. J Gastroenterol. 2021 Apr;56(4):336-349. doi: 10.1007/s00535-021-01765-4.

5. AbouSamra MM. Liposomal nano-carriers mediated targeting of liver disorders: mechanisms and applications. J Liposome Res. 2024 Dec;34(4):728-743. doi: 10.1080/08982104.2024.2377085.

6. Void-Holmes J, Cartee D. Blood-Borne and Related Pathogens. Infection Control in the Dental Office in the Era of COVID-19. 2024 Oct 14:27.

7. Watashi K, Urban S, Li W, Wakita T. NTCP and beyond: opening the door to unveil hepatitis B virus entry. Int J Mol Sci. 2014 Feb 19;15(2):2892-905. doi: 10.3390/ijms15022892.

8. Aslam H, Oza F, Ahmed K, Kopel J, Aloysius MM, Ali A, Dahiya DS, Aziz M, Perisetti A, Goyal H. The Role of Red Cell Distribution Width as a Prognostic Marker in Chronic Liver Disease: A Literature Review. Int J Mol Sci. 2023 Feb 9;24(4):3487. doi: 10.3390/ijms24043487.

9. Shiv Kumar Sarin1 • Ashok Choudhury1 • Manoj K. Sharma1 • Rakhi Maiwall1 • Mamun Al Mahtab2 • Salimur Rahman2 • Sanjiv Saigal3 • Neeraj Saraf3 • A. S. Soin3 etal . Acute-on-chronic liver failure: consensus recommendations of the Asian Pacifc association for the study of the liver (APASL): an update. Hepatology International (2019) 13:353–390.

10. Sarin SK, Choudhury A, Sharma MK, Maiwall R, Al Mahtab M, Rahman S, Saigal S, Saraf N, Soin AS, Devarbhavi H, Kim DJ, Dhiman RK, Duseja A, Taneja S, Eapen CE, Goel A, Ning Q, Chen T, Ma K, Duan Z, Yu C, Treeprasertsuk S, Hamid SS, Butt AS, Jafri W, Shukla A, Saraswat V, Tan SS, Sood A, Midha V, Goyal O, Ghazinyan H, Arora A, Hu J, Sahu M, Rao PN, Lee GH, Lim SG, Lesmana LA, Lesmana CR, Shah S, Prasad VGM, Payawal DA, Abbas Z, Dokmeci AK, Sollano JD, Carpio G, Shresta A, Lau GK, Fazal Karim M, Shiha G, Gani R, Kalista KF, Yuen MF, Alam S, Khanna R, Sood V, Lal BB, Pamecha V, Jindal A, Rajan V, Arora V, Yokosuka O, Niriella MA, Li H, Qi X, Tanaka A, Mochida S, Chaudhuri DR, Gane E, Win KM, Chen WT, Rela M, Kapoor D, Rastogi A, Kale P, Rastogi A, Sharma CB, Bajpai M, Singh V, Premkumar M, Maharashi S, Olithselvan A, Philips CA, Srivastava A, Yachha SK, Wani ZA, Thapa BR, Saraya A, Shalimar, Kumar A, Wadhawan M, Gupta S, Madan K, Sakhuja P, Vij V, Sharma BC, Garg H, Garg V, Kalal C, Anand L, Vyas T, Mathur RP, Kumar G, Jain P, Pasupuleti SSR, Chawla YK, Chowdhury A, Alam S, Song DS, Yang JM, Yoon EL; APASL ACLF Research Consortium (AARC) for APASL ACLF working Party.. Acute-on-chronic liver failure: consensus recommendations of the Asian Pacific association for the study of the liver (APASL): an update. Hepatol Int. 2019 Jul;13(4):353-390. doi: 10.1007/s12072-019-09946-3. Epub 2019 Jun 6. Erratum in: Hepatol Int. 2019 Nov;13(6):826-828. doi: 10.1007/s12072-019-09980-1.

11. Islam KU, Anwar S, Patel AA, Mirdad MT, Mirdad MT, Azmi MI, Ahmad T, Fatima Z, Iqbal J. Global Lipidome Profiling Revealed Multifaceted Role of Lipid Species in

Hepatitis C Virus Replication, Assembly, and Host Antiviral Response. Viruses. 2023 Feb 7;15(2):464. doi: 10.3390/v15020464.

12. Wang Y, Gao L. Cholesterol: A friend to viruses. Int Rev Immunol. 2024;43(4):248-262. doi: 10.1080/08830185.2024.2314577. Epub 2024 Feb 19. PMID: 38372266.

13. Pei J, Tian Y, Ye W, Han J, Dang Y, Cheng T, Wang W, Zhao Y, Ye W, Huangfu S, Li Y, Zhang F, Lei Y, Qian A. A novel recombinant ORF7-siRNA delivered by flexible nano-liposomes inhibits varicella zoster virus infection. Cell Biosci. 2023 Sep 12;13(1):167. doi: 10.1186/s13578-023-01108-1.

14. Yasamineh S, Kalajahi HG, Yasamineh P, Yazdani Y, Gholizadeh O, Tabatabaie R, Afkhami H, Davodabadi F, Farkhad AK, Pahlevan D, Firouzi-Amandi A, Nejati-Koshki K, Dadashpour M. An overview on nanoparticle-based strategies to fight viral infections with a focus on COVID-19. J Nanobiotechnology. 2022 Oct 8;20(1):440. doi: 10.1186/s12951-022-01625-0

15. Miao J, Gao P, Li Q, He K, Zhang L, Wang J, Huang L. Advances in Nanoparticle Drug Delivery Systems for Anti-Hepatitis B Virus Therapy: A Narrative Review. Int J Mol Sci. 2021 Oct 18;22(20):11227. doi: 10.3390/ijms222011227.

16. Maheshwari R, Kapoor D, Polaka S, Bhattacharya S, Prajapati B. Roadmap for Commercial Nanomedicine Development: Integrating Quality by Design Principles with Pharmaceutical Nanotechnology. Mol Pharm. 2025 Aug 4;22(8):4337-4372. doi: 10.1021/acs.molpharmaceut.5c00056.

17. Eskandari V, Mehmandoust S, Farahani Z, Mohammad NP, Hadi A. Liposomes/nanoliposomes and surfaced-enhanced Raman scattering (SERS): a review. Vibrational Spectroscopy. 2023 May 1;126:103536. DOI: 10.1016/j.vibspec.2023.103536

18. Damodaran A, Zachariah SM, Nair SC. Novel therapeutic approaches for the management of hepatitis infections. Ther Deliv. 2024 Mar;15(3):211-232. doi: 10.4155/tde-2023-0074.

19. Chen C, Liu J, Zhang H, Zhang H, Liang Y, Ye Q, Shen W, Luo H, Guo L. A Bait-and-Hook Hydrogel for Net Tumor Cells to Enhance Chemotherapy and Mitigate Metastatic Dissemination. *Pharmaceutics*. 2024; 16(12):1516. https://doi.org/10.3390/pharmaceutics16121516

20. Li M, Liu L, Li X, Li J, Zhao C, Zhao Y, Zhang X, He P, Wu X, Jiang S, Wang X, Zhang X, Wei L. Lipid Nanoparticles Outperform Electroporation in Delivering Therapeutic HPV DNA Vaccines. Vaccines (Basel). 2024 Jun 17;12(6):666. doi: 10.3390/vaccines12060666.

21. Haradhan Kumar Mohajan. (2025). Prevention of Hepatitis B Virus (HBV) Is Essential to Avoid Chronic Liver Disease. *nnovation in cience and echnology*, *4*(4), 112–121. etrieved from https://www.paradigmpress.org/ist/article/view/1658

22. Stroffolini T, Stroffolini G. A Historical Overview on the Role of Hepatitis B and C Viruses as Aetiological Factors for Hepatocellular Carcinoma. *Cancers*. 2023; 15(8):2388. https://doi.org/10.3390/cancers15082388

23. Nasser N, Tonnerre P, Mansouri A, Asselah T. Hepatitis-B virus: replication cycle, targets, and antiviral approaches. Curr Opin Virol. 2023 Dec;63:101360. doi: 10.1016/j.coviro.2023.101360

24. Pereira-Dutra FS, Teixeira L, de Souza Costa MF, Bozza PT. Fat, fight, and beyond: The multiple roles of lipid droplets in infections and inflammation. J Leukoc Biol. 2019 Sep;106(3):563-580. doi: 10.1002/JLB.4MR0119-035R

25. Pei J, Tian Y, Dang Y, Ye W, Liu X, Zhao N, Han J, Yang Y, Zhou Z, Zhu X, Zhang H, Ali A, Li Y, Zhang F, Lei Y, Qian A. Flexible nano-liposomes-encapsulated recombinant UL8-siRNA (r/si-UL8) based on bioengineering strategy inhibits herpes simplex virus-1 infection. Antiviral Res. 2024 Aug;228:105936. doi: 10.1016/j.antiviral.2024.105936.

26. Orosco, F. (2024). FROM NATURE'S PHARMACY TO SWINE HEALTH: HARNESSING NATURAL COMPOUNDS AGAINST PRRSV INFECTION. *Slovenian Veterinary Research*, *61*(1), 9–28. https://doi.org/10.26873/SVR-1789-2023

27. Singh, Latavia. An Architecturally-Configured Nanoparticulate System for Targeted Treatment of Hepatitis B Virus Infection. Sept. 2015, https://wiredspace.wits.ac.za/handle/10539/18542.

28. Anna Sak-Fong Lak. Hepatitis B Treatment: What We Know Now and What Remains to Be Researched. Hepatology communications. 2018, VOL. 0, NO. 0.

29. Cardoso RV, Pereira PR, Freitas CS, Paschoalin VMF. Trends in Drug Delivery Systems for Natural Bioactive Molecules to Treat Health Disorders: The Importance of Nano-Liposomes. Pharmaceutics. 2022 Dec 15;14(12):2808. doi: 10.3390/pharmaceutics14122808.

30. Fulton MD, Najahi-Missaoui W. Liposomes in Cancer Therapy: How Did We Start and Where Are We Now. *International Journal of Molecular Sciences*. 2023; 24(7):6615. https://doi.org/10.3390/ijms24076615

31. Li G, Dai Z, Guo J. Therapeutic Nanomaterials in NAFLD: Current Advances and Potential Applications in Patients with Concurrent HBV Infection. Int J Nanomedicine. 2025 Mar 25;20:3803-3823. doi: 10.2147/IJN.S510271.

32. Chandra P, Ruhela M, Kumar P, Porwal M, Verma A, Sharma H, Sachan N. Nanotechnology-based Approaches for Targeted Drug Delivery to the Small Intestine: Advancements and Challenges. Curr Pharm Des. 2025;31(24):1939-1957. doi: 10.2174/0113816128347722250109042022.

33. Wang Z, Du K, Jin N, Tang B, Zhang W. Macrophage in liver Fibrosis: Identities and mechanisms. Int Immunopharmacol. 2023 Jul;120:110357. doi: 10.1016/j.intimp.2023.110357. Epub 2023 May 22. PMID: 37224653.

34. Caddeo C, Miglionico R, Rinaldi R, Nigro I, Lamorte D, Chiummiento L, Lupattelli P, Funicello M, D'Orsi R, Valenti D, Santoro V, Fadda AM, Bisaccia F, Vassallo A, Armentano MF. PEGylated Liposomes Loaded with Carbamate Inhibitor ANP0903 Trigger Apoptosis by Enhancing ER Stress in HepG2 Cancer Cells. Int J Mol Sci. 2023 Feb 25;24(5):4552. doi: 10.3390/ijms24054552.

35. Ge D, An R, Xue L, Qiu M, Zhu Y, Wen G, Shi Y, Ren H, Li W, Wang J. Developing Cell-Membrane-Associated Liposomes for Liver Diseases. ACS Nano. 2024 Oct 29;18(43):29421-29438. doi: 10.1021/acsnano.4c12122.

36. Asandem DA, Segbefia SP, Kusi KA, Bonney JHK. Hepatitis B Virus Infection: A Mini Review. Viruses. 2024 May 3;16(5):724. doi: 10.3390/v16050724.

37. Vyas SP, Subhedar R, Jain S. Development and characterization of emulsomes for sustained and targeted delivery of an antiviral agent to liver. J Pharm Pharmacol. 2006 Mar;58(3):321-6. doi: 10.1211/jpp.58.3.0005.

38. Singh S, Vardhan H, Kotla NG, Maddiboyina B, Sharma D, Webster TJ. The role of surfactants in the formulation of elastic liposomal gels containing a synthetic opioid analgesic. Int J Nanomedicine. 2016;11:1475–82. doi: 10.2147/IJN.S100253.

39. Beck J, Reidenbach D, Salomon N, Sahin U, Türeci Ö, Vormehr M, Kranz L. mRNA therapeutics in cancer immunotherapy. Mol. Cancer. 2021;20:69. doi: 10.1186/s12943-021-01348-0.

40. Guevara M, Persano F, Persano S. Advances in lipid nanoparticles for mRNA-based cancer immunotherapy. Front. Chem. 2020;8:589959. doi: 10.3389/fchem.2020.589959.

41. Shobaki N, Sato Y, Suzuki Y, Okabe N, Harashima H. Manipulating the function of tumor-associated macrophages by siRNA-loaded lipid nanoparticles for cancer immunotherapy. J. Control. Release. 2020;325:235–248. doi: 10.1016/j.jconrel.2020.07.001.

42. Qiao L, Luo GG. Human apolipoprotein E promotes hepatitis B virus infection and production. PLOS Pathog. 2019;15 doi: 10.1371/journal.ppat.1007874.

43. Chung HJ, Chen X, Yu Y, Lee HK, Song CH, Choe H, et al. (2018). A critical role of hepatitis B virus polymerase in cirrhosis, hepatocellular carcinoma, and steatosis. FEBS Open Biol. 8, 130–145. doi: 10.1002/2211-5463.12357.

44. Choi Y.-M, Lee S.-Y, and Kim B.-J. Naturally occurring hepatitis B virus mutations leading to endoplasmic reticulum stress and their contribution to the progression of hepatocellular carcinoma. Int. J. Mol. Sci. 2019, 20:597. doi: 10.3390/ijms20030597.

45. Dimri, M., and Satyanarayana, A. Molecular signaling pathways and therapeutic targets in hepatocellular carcinoma. Cancers (Basel). 2020, 12:491. doi: 10.3390/cancers12020491.

46. D'souza, S., Lau, K. C., Coffin, C. S., and Patel, T. R. Molecular mechanisms of viral hepatitis induced hepatocellular carcinoma. World J. Gastroenterol. 2020, 26:5759. doi: 10.3748/wjg.v26.i38.5759.

47. Iannacone, M., and Guidotti, L. G. Immunobiology and pathogenesis of hepatitis B virus infection. Nat. Rev. Immunol. 2022, 22, 19–32. doi: 10.1038/s41577-021-00549-4.

48. Kim, G. W., Imam, H., Khan, M., Mir, S. A., Kim, S. J., Yoon, S. K., et al. HBV-induced increased N6 methyladenosine modification of PTEN RNA affects innate immunity and contributes to HCC. Hepatology. 2021, 73, 533–547. doi: 10.1002/hep.31313.

49. Lin, C. L., Chu, Y. D., and Yeh, C. T. Emergence of oncogenic-enhancing hepatitis B virus X gene mutants in patients receiving suboptimal Entecavir treatment. Hepatology (Baltimore, Md). 2019, 69:2292. doi: 10.1002/hep.30423.

50. Dorst DN, Boss M, Rijpkema M, et al. Photodynamic therapy targeting macrophages using irdye700dx-liposomes decreases experimental arthritis development. Pharmaceutics. 2021,13:1868. doi: 10.3390/pharmaceutics13111868.

51. Khan AA, Allemailem KS, Almatroodi SA, et al. Recent strategies towards the surface modification of liposomes: an innovative approach for different clinical applications. Biotech. 2020, 10:163. doi: 10.1007/s13205-020-2144-3.

52. Milani D, Athiyah U, Hariyadi DM, et al. Surface modifications of liposomes for drug targeting. In: Pathak YV, ed. Surface modification of nanoparticles for targeted drug delivery. Cham: Springer International Publishing. 2019, 207–20. doi: 10.1007/978-3-030-06115-9_11.

53. Pirmardvand Chegini S, Varshosaz J, Taymouri S. Recent approaches for targeted drug delivery in rheumatoid arthritis diagnosis and treatment. Artif Cells Nanomed Biotechnol. 2018, 46:502–14. doi: 10.1080/21691401.2018.1460373.

54. Ringhieri P, Mannucci S, Conti G, et al. Liposomes derivatized with multimeric copies of KCCYSL peptide as targeting agents for HER-2-overexpressing tumor cells. Int J Nanomedicine. 2017, 12:501–14. doi: 10.2147/IJN.S113607.

55. Santos MA, Goertz DE, Hynynen K. Focused ultrasound hyperthermia mediated drug delivery using thermosensitive liposomes and visualized with in vivo two-photon microscopy. Theranostics 2017, 7:2718–31. doi: 10.7150/thno.19662.

56. van Alem CMA, Metselaar JM, van Kooten C, et al. Recent advances in liposomal-based anti-inflammatory therapy. Pharmaceutics. 2021, 13:1004. doi: 10.3390/pharmaceutics13071004.

57. Malik S, Muhammad K, Waheed Y. Nanotechnology: A Revolution in Modern Industry. *Molecules*. 2023, 28(2):661. https://doi.org/10.3390/molecules28020661

58. Shafique M, Luo X. Nanotechnology in Transportation Vehicles: An Overview of Its Applications, Environmental, Health and Safety Concerns. Materials (Basel). 2019 Aug 6;12(15):2493. doi: 10.3390/ma12152493.