

Drug Discovery and Vaccine Development in Viral Hepatitis: An Overview

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Abstract

Viral hepatitis continues to be a prime health challenge globally, leading to significant mortality due to hepatic inflammation, cirrhosis and hepatic carcinoma. It is classified into 5 variants, namely Hepatitis A-E, depending on the causative virus variants. Our review summarises the incidence of viral hepatitis, its variants and elucidates the advances made in the field of drug discovery and vaccine development against hepatitis viruses. Hepatitis drug discovery has evolved from conventional immunotherapies to direct-acting antivirals. Significant developments in the understanding of viral entry inhibition, disruption of viral capsid assembly, viral RNA downregulation and efficient regulation of host-virus interactions have contributed to the birth of newer drug therapies for hepatitis. However, the viral genetic composition has posed a barrier to therapy development. The contribution of hepatitis vaccines also has taken centre stage in the treatment of hepatitis. Even though they have demonstrated good clinical efficacy, they have been ineffective in patients infected with hepatitis. This has led to the development of therapeutic vaccines that have shown significant benefits in infected individuals. Corroborating this evidence, we believe that even though the existing drug therapies have managed to reduce the incidence of Hepatitis, further research in this direction is warranted.

Keywords: Hepatitis, Inflammation, Vaccines, Drug Discovery, Interferon alpha

1. Introduction

The rise of inflammatory diseases globally has emerged as a serious concern for mankind. One such disease, namely hepatitis, has garnered immense attention due to its severe epidemiological attributes. Hepatitis refers to inflammation of the liver that may result from viral infections and, in cases of chronic infection, lead to fibrosis of the liver and cirrhosis, with subsequent liver cancer [1]. Five major hepatotropic viruses, namely Hepatitis A virus (HAV), hepatitis B virus (HBV), hepatitis C virus (HCV), hepatitis D virus (HDV), and hepatitis E virus (HEV), are recognised as the principal causes of viral hepatitis. Among these, chronic HBV and HCV infections constitute a major worldwide health burden owing to their high prevalence and their ability to cause progressive liver disease, cirrhosis, hepatocellular carcinoma, and premature death. As per the reports of the World Health Organization (WHO), the toll of HBV and HCV reached an astounding figure of 304 million globally in the year 2022, with 2.2 million patients diagnosed with new cases of Hepatitis B and Hepatitis C. A staggering 1.3 million lost their lives following HBV and HCV infection in 2022 [2]. As per the Global Hepatitis Report 2026 published by WHO, nearly 3% of the global population, accounting for approximately 287 million people, were diagnosed with HBV and HCV in 2024. Collectively, HBV and HCE caused mortality in nearly 1.3 million people worldwide in 2024. Similarly, as per WHO, 40 million Indians adults have been diagnosed with HBV and 6-12 million people with HCV, while HAV is predominant in children[3]. These epidemiological figures not only depict the magnitude of disease outbreaks but also eagerly call for strategic

disease diagnosis, newer drug discovery, and efficacious, cost-effective and accessible therapeutics for the ailing population.

The evolution of drug discovery has been the driving force for effective disease management in ailing individuals. Until the start of the 19th century, drug discovery was often accidental or by chance. The therapeutic agents mainly comprised natural sources of plant or animal origin [4]. Eventually, from the advent of the 19th century, drug discovery saw a new horizon in synthetic drug discovery [5]. The earliest known development in hepatitis drug discovery was the discovery of interferon alpha in 1980, before which the treatment mainly included bed rest [6]. Current modern drug discovery has managed to accelerate the drug discovery process, inculcating a multidimensional approach by employing advanced technology like Artificial Intelligence (AI) in computer-aided drug designing, in silico studies, pre-clinical studies, clinical trials, etc. [7]. Drug discovery for hepatitis, especially HBV and HCV, has evolved from nonspecific immune modulators (interferons) to highly targeted direct-acting antivirals (DAAs) that now cure >90% of HCV cases and durably suppress HBV in most patients, mainly including entry inhibitors, capsid assembly modulators, siRNA, antisense oligonucleotides, and nucleic acid polymers (NAPs) [8]. Concurrently, advances in immune-based approaches like vaccine development and monoclonal antibodies have significantly contributed to hepatitis therapeutics.

Thus, our review article attempts to corroborate the evidence of the various drug discoveries that have led to the development of therapeutics for viral hepatitis. It also highlights the different kinds of vaccines available for viral hepatitis.

2. Hepatitis

Hepatitis is an inflammatory condition of the liver occurring due to viral infection, though it can also result from alcohol, toxins, autoimmune disease, and metabolic disorders. Depending on the causative agents, it is either characterised as Viral Hepatitis or Non-viral Hepatitis [9]. Viral Hepatitis is a major health concern because it is both common and potentially severe. Acute hepatitis can cause fever, fatigue, jaundice, nausea, abdominal pain, and in some cases acute liver failure. Certain forms of hepatitis may also develop into a chronic stage, where the virus persists in the body for years or decades [2]. During that time, the immune system continues to attack infected liver cells, causing ongoing inflammation. Repeated inflammation leads to fibrosis, and fibrosis can progress to cirrhosis, liver failure, and cancer [10].

2.1 Variants of Viral Hepatitis

Viral hepatitis is broadly classified into 5 different categories, namely Hepatitis A (caused by HBA), Hepatitis B (caused by HBV), Hepatitis C (caused by HCV), Hepatitis D (caused by HDV) and Hepatitis E (caused by HEV) [11].

2.1.1 Hepatitis A

Hepatitis A is caused by HAV and is mainly spread through the fecal–oral route, particularly through unclean food and water sources or close contact with infected individuals. HAV infection generally causes an acute illness and not chronic hepatitis [12]. Identification of anti-HAV IgM antibodies can help in the diagnosis of acute infection, and vaccination represents an effective preventive strategy. Hepatitis A spreads easily, but it is preventable. Vaccination is highly effective in preventing hepatitis A [13].

2.1.2 Hepatitis B

Hepatitis B can lead to both acute and chronic hepatitis. It spreads mainly through infected blood and semen. Upon exposure, HEV primarily attacks the hepatocytes [14]. Chronic hepatitis B and C can remain silent for years while gradually impacting the liver. By the time symptoms become obvious, many patients already have significant fibrosis, cirrhosis, or even hepatocellular carcinoma [15]. Serological assays can detect Hepatitis B Surface Antigen (HBsAg). Further steps involve investigating the HBV virion concentration and identifying the genotypic variants of HBV in infected individuals [16].

2.1.3 Hepatitis C

Hepatitis C mainly spreads due to exposure to infected blood. Common risks include unsafe injections, sharing needles, and unscreened blood products. Many infected people have no symptoms for years, which makes the disease hard to detect [17]. Chronic HCV is known to commonly cause hepatocellular carcinoma through liver cirrhosis [18]. Previously, pegylated interferon (PEG-IFN) and ribavirin therapies have shown promising results in reducing HCV in patients [19]. Recently, a remarkable breakthrough in HCV diagnosis has emerged through RNA evaluation techniques that can efficiently detect HCV in infected [20].

2.1.4 Hepatitis D

What makes Hepatitis D quite interesting is that HDV can infect only those individuals who have had Hepatitis B previously [21]. This primarily happens because HDV requires the surface antigens of HBV for it to assemble and proceed with secretion [22]. It spreads through blood and body fluids in a way similar to hepatitis B. The severity of liver damage in Hepatitis D is much greater than Hepatitis B. It can speed up cirrhosis and rapidly progress towards liver failure. Symptoms may include tiredness, jaundice, and abdominal discomfort. Diagnosis usually requires specific blood testing for the HDV antigen [23]. HDV therapies have been mediated through interferons, lipopeptides, nucleotide analogues, etc that have shown promising results [24].

2.1.5 Hepatitis E

Hepatitis E is a viral form of hepatitis that usually spreads through contaminated water. It is prevalent in regions of improper sanitation and contaminated drinking water. The virus spreads by the faecal-oral route. Symptoms can include fever, tiredness, nausea, abdominal pain, and jaundice [25]. HEV can be diagnosed by direct detection of HEV RNA or the antigens of its viral capsid. The indirect methods of HEV detection often include the measurement of anti-HEV antibodies circulating in the blood [26]. Therapies including T cells, interferons and ribavirin have shown promising results in reducing viral loads of HEV [27].

Collectively, the above evidence emphasises the substantial global prevalence and gravity of viral hepatitis, highlighting the urgent need for advanced innovative drug discovery and vaccine development. Continued efforts in these areas have been made to discover novel drug targets and therapies, including vaccines to mitigate hepatitis and are discussed in the section below.

3. Drug Discovery in Hepatitis

Antiviral drug discovery for hepatitis has been closely associated with advances in molecular virology, assessment of structural aspects of the hepatitis viruses, supported by medicinal chemistry, and the understanding of how viruses react with host organisms [28]. Identification of essential viral enzymes, structural proteins, replication complexes, cellular receptors, and host dependency factors has enabled the development of targeted antiviral agents [8].

Bulevirtide, lonafarnib, and REP 2139 are among the best-known investigational or emerging therapeutics in the field of hepatitis. Studies report that combinations with pegylated-interferon alpha (PEG-IFN- α) can improve outcomes, but long-term efficacy and tolerability are yet to be determined. REP 2139, especially with PEG-IFN- α , has shown promising results in the preliminary studies [29, 30].

3.1 Hepatitis A

In HEV cases, corticosteroid therapy and agents like AZD 1480, heme oxygenase-1 (HO-1), and also zinc chloride have shown viral load reduction [31]. A Janus kinase (JAK) inhibitor, namely AZD1480, has shown inhibition of HAV replication, most likely by interfering with cellular pathways involved in viral IRES-mediated translation. Another candidate, zinc chloride, has shown antiviral activity against HAV in *in vivo* experiments, speculated to target host cellular processes involved in viral replication. The pharmacological induction of HO-1 has also been investigated as a potential host-targeted approach owing to its ability to reduce HAV replication *in vitro* [32]. Further, the identification of host factors as essentials of viral replication has been critical in HAV drug discovery. Alternately, understanding of the cellular components involved in the post-transcriptional modification and stability of HAV RNA has led to discovering potential targets for host-directed antiviral development. This offers greater benefits as hosts are less prone to the rapid genetic variation that can lead to resistance against virus-specific drugs. Development of safe and effective antiviral therapy could synergise with corresponding vaccination strategies, particularly for severe HAV infection, although deeper research and clinical validation are mandatory before these experimental approaches become approved therapies [33].

3.2 Hepatitis B

Interferon-based therapy was one of the major therapeutic strategies for HBV. It was the first approved therapy for chronic HBV, triggering activation of the immune system, with moderate action and unfortunately significant toxicity [34]. Conventional interferon- α (IFN- α) and PEG-IFN- α promote immunomodulatory signalling, further activating intracellular antiviral pathways instead of HBV polymerase inhibition. In the case of finite treatment options, PEG-IFN is the choice of drug for patients [35]. PEG-IFN- α can induce sustained virological responses and loss of HBsAg with seroconversion [36]. However, its clinical utility is retarded by variable efficacy and a considerable adverse-effect profile, including influenza-like symptoms, cytopenias, neuropsychiatric manifestations, and autoimmune complications. Treatment response is also influenced by viral genotype, baseline viral load, and host-related factors. Despite these limitations, PEG-IFN- α remains clinically relevant because it can promote durable immune-mediated control of HBV replication after treatment discontinuation [37]. Concurrently, the interferon therapy has promoted the development of HBV drug-discovery strategies, using a combination of DAAs and immunomodulators to obtain efficient viral load reduction. The presence of covalently closed circular DNA (cccDNA) and integrated HBV DNA is one of the leading causes for failure of current therapies. Nucleos(t)ide analogues (NAs) are successful in long-term HBV suppression with optimised control of hepatitis and its progression [38]. NAs like lamivudine, adefovir, entecavir, and tenofovir target HBV reverse transcriptase, which suppresses viral DNA replication effectively [15, 39]. Entecavir or tenofovir (TDF/TAF) therapy suppresses HBV DNA, reduces cirrhosis risk, and is recommended for indefinite or long finite drug therapies. Functional cure (HBsAg loss) remains uncommon with NAs alone. Investigation of novel agents (siRNA, antisense, capsid assembly modulators, immunotherapies) is in the pipeline to raise the HBsAg loss rate rather than just suppression [40]. Sodium taurocholate co-transporting polypeptide (NTCP) functions as a critical receptor for entry of HBV in the host. Blocking the interaction between HBV and NTCP could

suppress infection of hepatocytes with HBV. Bulevirtide, a synthetic lipopeptide, binds to NTCP and prevents entry of HBV and HDV into the hepatocytes. Bulevirtide has been particularly developed for chronic HDV infection, which depends on HBV envelope proteins for viral assembly and propagation [41]. Bepirovirsen, an antisense oligonucleotide, and VIR-2218 (elebsiran), an RNA interference therapy, have both demonstrated efficient reduction in HBsAg in clinical trials [4]. Similarly, capsid assembly modulators like JNJ-6379 disrupt the viral shell, preventing packaging of the genetic material of the virus. The HBV cccDNA plays a major role in the gene transcription of HBV. Its silencing using CRISPR technology could further boost HBV therapeutics [42]. Newer approaches like RNAi-based therapies also have demonstrated abilities to reduce HBV antigen production. Small interfering RNAs (siRNAs) are designed to target HBV RNA transcripts and promote their degradation through the RNA-induced silencing complex. Several siRNA-based candidates such as JNJ-3989 and AB-729 are currently being tested clinically [43, 44]. These approaches are being investigated either as monotherapy or in combination with NAs and immune modulators [45, 46]. NAPs are synthetic phosphonothioate oligonucleotide-like compounds shown to interfere with HBV particle assembly and secretion. REP 2139 and related NAPs have shown promising results in early clinical studies, particularly when combined with tenofovir and PEG-IFN- α , while few studies demonstrated decline in HBsAg and HBsAg loss in certain patients [47, 48].

3.3 Hepatitis C

For HCV, the early therapies included PEG-IFN- α and ribavirin; however, the response was limited to genotype 1. This led to the discovery of further virus-specific targets [49, 50]. Subsequently, drug discovery relied on deepening knowledge of the replication cycle and then blocking viral functions. A shift from broad immune stimulation to mechanism-based inhibition produced higher cure rates, shorter courses, and far better tolerability [51]. Before the advent of DAA, treatment for HCV consisted of ribavirin, with results showing sustained virologic response (SVR) rates of nearly 40–50% in HCV patients (genotype 1) and substantial treatment-related adverse effects. Subsequently, deep analysis of the HCV replication cycle and the structural and functional characteristics of virus proteins, especially the NS3/4A serine protease, NS5A replication complex, and NS5B RNA-dependent RNA polymerase, boosted the rational development of virus-specific DAAs [52]. Protease inhibitor-based regimens emerged from NS3/4A drug-discovery programs and were among the first targeted HCV therapies [53]. Even though the NS3/4A protease inhibitors boceprevir and telaprevir improved treatment outcomes, they were associated with greater toxic effects and associated with complex treatment therapies. Subsequent generations of protease inhibitors, such as simeprevir, grazoprevir, glecaprevir, and voxilaprevir, demonstrated improved potency and tolerability [54]. NS5A inhibitors, including daclatasvir, ledipasvir, velpatasvir, and pibrentasvir, provided highly potent inhibition of viral replication and assembly. Interestingly, the NS5B polymerase inhibitors, particularly the nucleotide analogue sofosbuvir, have shown effective and broader antiviral activity and a high barrier to resistance [55]. Combination therapies of drugs like sofosbuvir + velpatasvir and glecaprevir + pibrentasvir are highly effective against all genetic variants, while sofosbuvir + velpatasvir + voxilaprevir is better suited for patients needing re-treatment. A dosage regimen for DAA includes oral treatment for 8–12 weeks to obtain an SVR rate greater than 95%, with substantially better tolerability than interferon-based therapy [56–58]. Further, multiple efforts have been made to understand the antivirals targeting the host and also inhibitors which prevent virus entry [59]. Cellular factors involved in HCV entry, including CD81, scavenger receptor class B type I (SR-BI), occludin, and claudin-1, have shown promising therapeutic benefits. Other host-directed strategies have explored molecules such as miR-122 inhibitors, cyclophilin inhibitors, and agents

targeting host lipid metabolism, although these approaches remain less clinically advanced than virus-specific DAAs [60].

3.4 Hepatitis D

HDV has historically had very limited treatment options, with interferon-based therapy being the mainstay for decades. That said, recent years have brought a notable drug-discovery surge, with new targets and new agents that exploit the HDV dependence on HBV and host pathways. HDV drug discovery has evolved from interferon-based immunomodulation toward mechanism-based strategies targeting viral entry, assembly, and host–virus interactions[61]. As HDV depends on HBV for its envelope, the development of HDV-specific therapies has historically been challenging, and treatment strategies have increasingly focused on targeting viral entry, subsequent replication, assembly, and interactions with the host [62]. Therapeutic approaches involving entry inhibition, prenylation inhibition, and nucleic acid polymers are especially important development directions [63]. The identification of NTCP as the cellular receptor for HBV/HDV entry enabled the development of bulevirtide, an entry inhibitor that blocks viral entry into hepatocytes, while understanding the requirement for prenylation of large hepatitis D antigen (L-HDAg) led to the development of the farnesyltransferase inhibitor lonafarnib, which interferes with HDV particle assembly and release [64]. Additionally, nucleic acid polymers, antisense oligonucleotides, and immune-modulatory strategies also showed beneficial effects. The combination of agents targeting distinct stages of the HDV life cycle represents a promising strategy for achieving durable viral suppression and improving long-term clinical outcomes [65]. The large hepatitis D antigen (L-HDAg) has garnered attention in HDV drug discovery. It undergoes post-translational farnesylation (prenylation), a host-mediated modification that is essential for interaction with HBV envelope proteins and subsequent incorporation of HDV ribonucleoprotein complexes into newly formed viral particles [66]. This process led to the development of prenylation inhibitors, which prevent the farnesylation of L-HDAg and consequently interfere with HDV assembly and release. Lonafarnib, an orally active farnesyltransferase inhibitor, is the most advanced compound in this class. Clinical studies have demonstrated that lonafarnib can reduce HDV RNA levels, supporting the importance of L-HDAg prenylation as a therapeutic target. However, gastrointestinal adverse effects and dose limitations have encouraged investigation of combination regimens, including the use of ritonavir to increase lonafarnib exposure [67]. Similar to HBV, the therapeutics for HDV also include NAPs like REP 2139 and REP 2165. These compounds are thought to interfere with the secretion or assembly of HBV subviral particles and may consequently affect the availability of HBsAg required for HDV particle production and release[65].

3.5 Hepatitis E

To date, there is no approved HEV-specific direct-acting antiviral drug. However, Ribavirin, a broad-spectrum guanosine analogue, is mainly used for chronic HEV infection, particularly in patients with lowered immunity. The therapy of HEV mainly relies on ribavirin, while PEG-IFN- α in some studies have shown otherwise [68]. Another interesting target for HEV therapy is HEV RNA-dependent RNA polymerase (RdRp), where DAAs can prevent viral RNA replication. Nucleoside and nucleotide analogues can potentially interfere with viral RNA synthesis, with the nucleotide analogue sofosbuvir demonstrating inhibitory activity against HEV replication *in vitro* [69]. Similarly, Sofosbuvir, a nucleotide analogue originally developed for HCV, has attracted particular interest because of its ability to inhibit *in vitro* HEV replication and even in clinical studies. On the contrary, as previously mentioned, its clinical efficacy against HEV remains questionable, due to which it is not included as a standard HEV therapy [70]. Cyclophilin inhibitors have been able to achieve efficient antiviral activity against HEV in experimental studies with

a host-directed strategy. This could offer a better advantage in terms of resistance to viral influence; however, its toxicity and effects on normal cellular functions pose a greater challenge [71]. Silvestrol is derived from *Aglaia* species and has proven to be a potential candidate for HEV downregulation in experimental models. It inhibits the cellular RNA helicase eIF4A, which is involved in the initiation of the translation process. Laboratory studies have shown that Silvestrol can inhibit HEV replication, hinting that host translation machinery could serve as a potent antiviral target [72]. PEG-IFN- α has been employed in chronic HEV cases, especially in liver transplant cases, although it carries the risk of graft rejection and other adverse effects. However, PEG-IFN- α may have antiviral activity in cases of non-transplant, but clinical evidence is limited, and treatment outcomes are variable [27].

4. Vaccine Development in Viral Hepatitis

Vaccination has contributed as an effective strategy for preventing viral hepatitis. Currently, highly effective prophylactic vaccines are available against HAV and HBV, while HBV vaccination also provides indirect protection against HDV. However, the absence of a licensed HCV vaccine and limited global access to HEV vaccination remain important challenges for hepatitis prevention and elimination.

4.1 Hepatitis A

There are three approved HAV vaccines, including the inactivated combination vaccine Twinrix and single-antigen vaccines Havrix and Vaqta [73, 74]. Twinrix contains an inactivated HAV antigen along with recombinant HBsAg and offers protection against HAV and HBV. These vaccines have demonstrated high efficacy in preventing symptomatic HAV infection and have contributed substantially to reductions in disease incidence and outbreak control [75]. Another type of Vaccine discovery includes live attenuated HAV vaccines, where there is genetic and phenotypic attenuation of viruses, which offer reduced replication rates and do not lead to hepatitis. The H2 and LA-1 strains belong to this category. However, the greater challenge in using such vaccines in comparison with inactivated vaccines is the concern of their stability and the control of the rate of viral replication. Another kind of vaccine shown to have efficacy in cases of HAV is based on an inactivated phospholipid virosome named Epaxal [76]. It has demonstrated optimum clinical efficiency in patients obtaining seroprotection often after a fortnight of administration [77].

4.2 Hepatitis B

The discovery of HBV vaccine marks the greatest achievement in the field of Hepatitis vaccines. Hepatitis B vaccination has since been recognised as the first vaccine capable of preventing a human cancer, given the strong causal link between chronic HBV infection and hepatocellular carcinoma [78]. Historically, the earliest HBV vaccine was obtained from purified HBsAg of infected individuals, which was eventually replaced with HBsAg obtained from recombinant DNA technology. HBV vaccination strategies comprise either universal vaccination in all infants or selective vaccine therapy using HBV vaccine and HBIG, especially in mothers exposed to HBV, to prevent their newborns from infection[79]. HBV vaccines induce protective anti-HB antibodies and provide highly effective protection against acute and chronic HBV infection. Studies have shown a significant drop in HBV infection and its associated liver cirrhosis [80]. In 2021, a recombinant Hepatitis B vaccine named Prehevbrio was approved by the United States Food and Drug Administration (US-FDA) and subsequently withdrawn owing to reasons not related to vaccine safety or efficacy [81]. The currently known vaccine for HBV includes Engerix-B, Recombivax HB and Heplisav, offering greater immunogenicity and convenient dosage schedules in patients, while newer formulations such as Heplisav-B, which incorporates the CpG 1018 adjuvant, have been developed to enhance immunogenicity and

permit a simplified two-dose schedule in adults [82]. Another novel vaccine named Fendrix, containing an adjuvant system designed to improve immune responses, is used in selected populations, including patients with altered renal function [83]. Another category of HBV vaccines includes a therapeutic vaccination strategy which is used in individuals already infected with chronic HBV infection. These are an important category of vaccines as the other prophylactic vaccines are deemed ineffective in individuals with existing HBV infection[84]. The known therapeutic vaccines for HBV include GS-4774 (Tarmogen). It is known to stimulate HBV-specific T-cell responses and is obtained from yeast through recombinant technology. Similarly, TG1050 is known to express HBV antigens and is prepared using modified vaccinia Ankara (MVA). These candidates have offered greater immunogenicity, but their ability to significantly clear the HBsAg to enhance its therapeutic benefit is still yet to be identified [85].

4.3 Hepatitis C

Even though the discovery of a hepatitis vaccine is moving at a rapid pace, the world awaits the introduction of a licensed HCV vaccine [86]. One of the contributing factors could be the high incidence of genetic variability. Interestingly, the HCV vaccine research has focused on the envelope glycoproteins, namely E1 and E2, known for mediating the attachment and entry of viral components in the hepatocytes [87]. Incorporation of MF59 with E1/E2 protein vaccines employing recombinant technology has offered better immunogenicity in preclinical and clinical outcomes. They have been able to induce antibodies with capacities to neutralise HCV with multiple genotypic constitutions [88]. Serious efforts have also been made in the development of recombinant chimpanzee adenovirus serotype 3 (ChAd3) vector along with a modified vaccinia Ankara (MVA) vector, which have aimed to enhance T-cell mediated actions leading to effective recognition of HCV and promote its clearance[89]. Its clinical efficiency has also been demonstrated to alter the viral kinetics but unfortunately has failed to prevent HCV infection [90].

4.4 Hepatitis D

The world currently awaits a dedicated vaccine specifically targeting HDV. Concurrently, it is known that for HDV to proliferate, the presence of HBsAg is crucial. This suggests that the vaccination strategy for HBV is currently the therapy to prevent the occurrence of HDV infection [29]. However, it is worthwhile to note that individuals infected with HBV and administered with HBV vaccine may not always be protected from concurrent HDV infection. It is proposed that the development of an HDV vaccine could theoretically target HDV-specific antigens [91]. These antigens could mainly include the small Hepatitis D antigens (S-HDAg) and also the large Hepatitis D antigens (L-HDAg). Evidence suggests that vaccines combining both HBsAg and HDAg could prevent HDV infection, but further studies are warranted [92].

4.5 Hepatitis E

The first HEV vaccine candidate reported to have shown good clinical efficacy was rHEV, but subsequently no development was reported [93]. Subsequently, another interesting development in the field of HEV occurred with the discovery of the HEV 239 (Hecolin) vaccine. This vaccine is capsid protein oriented and is prepared using recombinant technology. It is the only licensed HEV vaccine available. It involves the ORF2 protein and functions by triggering antibodies and protecting against HEV. In a clinical setup, it has shown remarkable efficiency and a desirable safety profile [94]. While Hecolin is the primary vaccine used currently, further research on other HEV vaccines like Lipo-NEP and HEV P179 is in the pipeline [95].

5. Conclusion

Viral hepatitis has been recognised as a major global health issue, often leading to chronic inflammation of the liver followed by cirrhosis, hepatic carcinoma and subsequently death. The contribution of advances in the understanding of Hepatitis A-E has led to the upliftment of drug discovery from mere non-specific immunomodulatory techniques to rather specific target-based antiviral therapies. Major contributors to hepatitis drug discovery include agents like direct-acting antivirals, nucleoside analogues, and pegylated interferons that have offered efficient relief in infected individuals. New research has been aligned in the direction of targeting viral entry inhibition, disruption of viral capsid assembly, viral RNA downregulation and efficient regulation of host-virus interactions. One of the challenges in hepatitis drug discovery has been the presence of cccDNA acting as a central template for reducing the efficiency of antiviral drugs. This has brought significant attention to the importance of developing hepatitis vaccines. Traditionally, vaccines have been used mainly for prophylactic purposes, but have failed to offer protection in infected individuals. This has shed light on the recent advances in therapeutic vaccines with a promising effect in infected individuals as well. While existing drug discovery and vaccine development have managed to provide relief from different forms of hepatitis globally to a certain extent, there is a definite need for even more research in this direction.

6. References:

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