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Hepatitis C virus vaccine development: Current status and future prospects

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Abstract

Hepatitis C is a serious liver infection caused by the Hepatitis C Virus (HCV), which spreads mostly through contact with contaminated blood. This review looks at the worldwide health implications of HCV, which affects millions and can cause severe liver disorders like cirrhosis and liver cancer. Unlike Hepatitis A and B, there is no vaccine for Hepatitis C, making preventive measures critical. The study discusses the historical context of hepatitis discovery, the detection of HCV in 1989, and the progression of treatment options. Current advances in Direct-Acting Antiviral (DAA) treatments have changed HCV treatment, allowing for significant cure rates. Despite these advances, issues like as treatment accessibility and the need for better screening approaches remain. On-going research aims to improve global treatment access and identify viable vaccine candidates to prevent HCV infection.

Keywords: Hepatitis C, Hepatitis C Virus (HCV), liver infection, blood transmission, Direct-Acting Antivirals (DAAs)

Introduction

Hepatitis C is an infection of the liver caused by the Hepatitis C Virus (HCV), a blood borne pathogen that primarily affects the liver. Transmission occurs mainly through contact with infected blood, most commonly through sharing of needles among drug users. HCV is an important global health issue, with millions of people suffering with chronic Hepatitis C, which can lead to catastrophic liver diseases such as cirrhosis and liver cancer (WHO, 2024) [38]. Despite the availability of vaccines for Hepatitis A and B, there is at present no vaccine for Hepatitis C, hence preventive measures are crucial. However, recent developments in antiviral therapies have made it possible to cure the majority of HCV patients, emphasizing the importance of early identification and treatment (Kim *et al.*, 2016, Mayo Clinic, 2023) [20, 24].

The history of hepatitis is distinguished by the gradual detection of various kinds of the disease, each caused by a unique virus. The term "hepatitis" was initially used to refer to general liver inflammation, but particular viral causes were not identified until the middle of the twentieth century. Hepatitis A and B were first identified in the 1940s and 1960s, accordingly. With Their processes of transmission and effects on the liver are gradually becoming more understood. Hepatitis C, originally described as "non-A, non-B hepatitis," was first identified in 1989, resulting in important advances in understanding chronic liver illness. In recent years, research and development of effective hepatitis C treatments, particularly Direct-Acting Antivirals (DAAs), has changed disease management. Despite these advances, the global burden of hepatitis remains large, with on-going efforts to completely eliminate viral hepatitis as a public health threat by 2030 (WHO Cholongitas *et al.*, 2022, Chen & Morgan, 2023) [9, 8].

What is hepatitis?

Hepatitis is a general term for liver inflammation this can be caused by a variety of factors like viral infections, consumption of alcohol, toxins, certain drugs, and autoimmune disorders. Hepatitis A, B, C, D, and E are the most common types of viral hepatitis, with each caused by a different virus and that range in severity and path of transmission. Hepatitis can be classified as acute, which is a quick outbreak of inflammation that disappears on its own, or chronic, which is an on-going condition of inflammation that can cause catastrophic

liver damage, including cirrhosis and liver cancer. Depending on its cause, hepatitis can appear with a wide range of symptoms, from moderate to severe, or even asymptomatic in some cases. Depending on the origin,

hepatitis may present with a wide range of symptoms, from moderate to severe, or even asymptomatic in certain situations (CDC, 2023, Mayo Clinic, 2023) [4, 25].

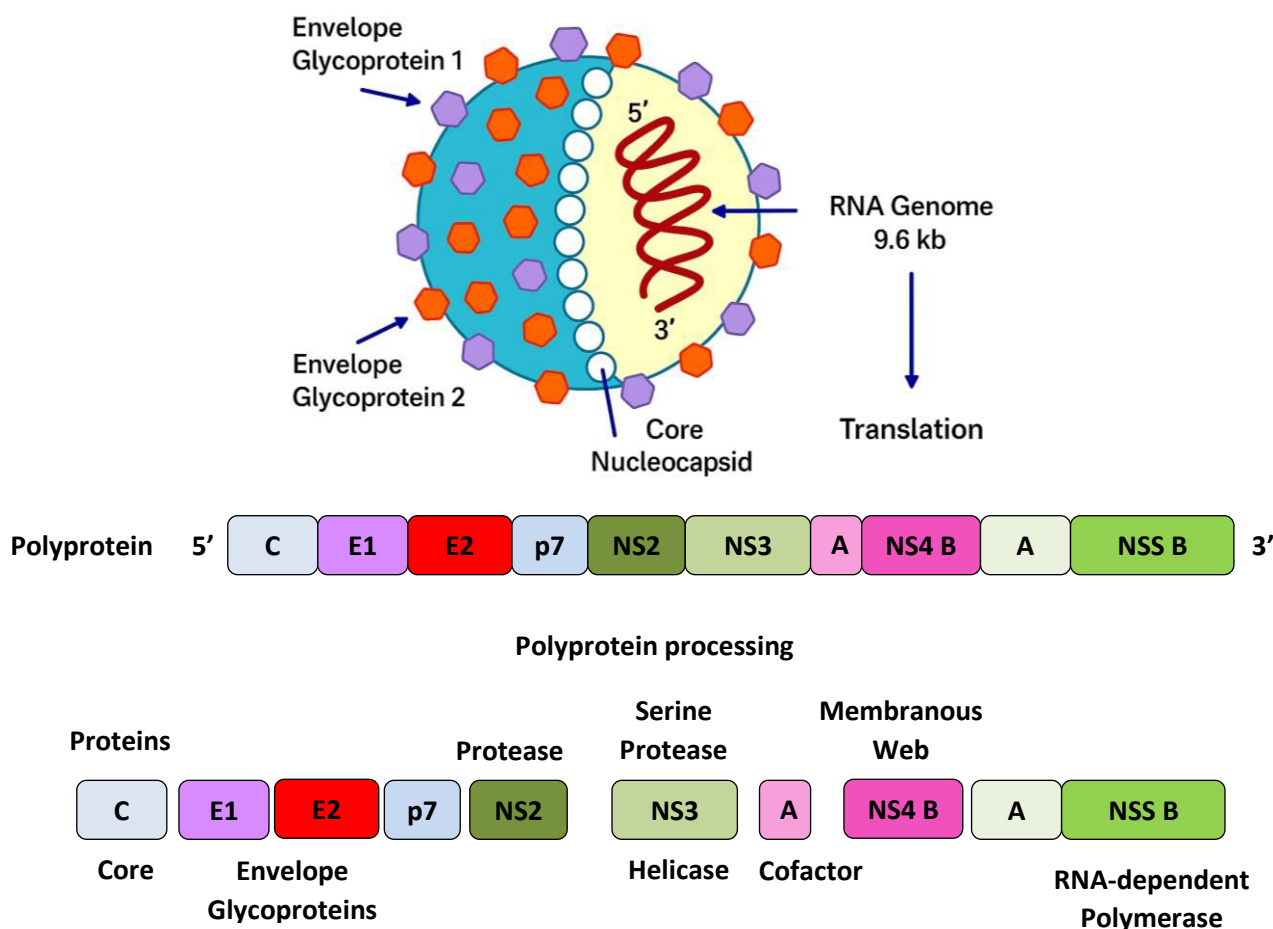


Fig 1: Structure of hepatitis c virus (Antiviral Res, 2003)

Genomic region and structure

Hepatitis C Virus (HCV) is an included virus with a positive-sense, single-stranded RNA genome. The HCV genome is around 9.6 kb in size and encodes a single poly protein, which is subsequently divided into structural and non-structural proteins. The viral genome is constructed up of a 5'untranslated region (UTR), followed by a coding sequence containing the core, envelope (E1 and E2), and non-structural (NS) proteins, and a 3' UTR. The structural

proteins, core and envelope proteins, are critical for virus assembly and entry into host cells, whereas non-structural proteins are required for viral replication and immune evasion. Recent research have documented the great diversity of the E1 and E2 envelope proteins, which contribute to the virus's the capacity to escape immune responses and complicate vaccination. (Graham *et al.*, 2023, Kawaoka *et al.*, 2023, Vignuzzi *et al.*, 2023) [13, 19, 35].

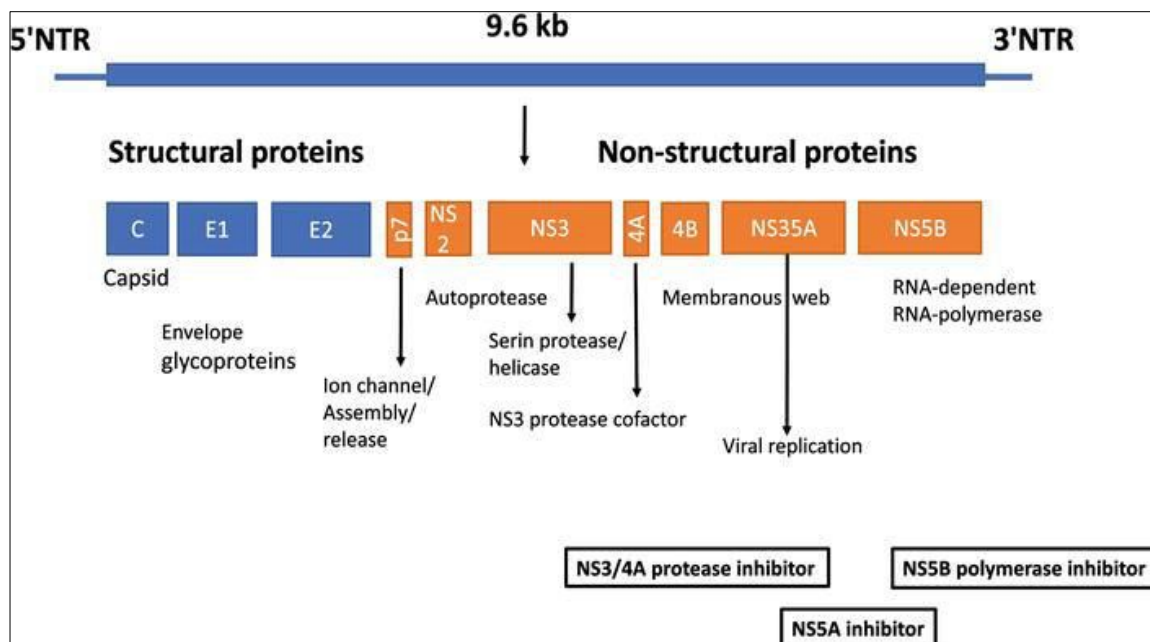


Fig 2: HCV Proteins (Deniz & Akhan, 2023) ^[32]

Problems and causes by HCV

Hepatitis C Virus (HCV) provides serious health risks while it can generate chronic liver disease that includes cirrhosis and cancer of the liver. The primary cause of HCV infection is exposure to infected blood, often through sharing needles among people who inject drugs, getting contaminated blood products, or, less usually, through other routes such as needle-stick injuries or transmission from an infected mother to her baby during birthing (WHO, 2023, CDC, 2023) ^[4]. Despite the success of antiviral medicines, the global burden of HCV remains high due to a number of factors, including the asymptomatic character of chronic infection, which commonly results in delayed identification, the high cost of treatment, and the difficulties of reaching high-risk populations. Recent studies highlight the difficulties of HCV care, including the rise of treatment-resistant viral strains and the need for more screening and prevention methods to reduce transmission rates (Smith *et al.*, 2023, Brown *et al.*, 2023) ^[30, 2]. HCV is less typically transferred through sexual contact, although it can occur, particularly among those with multiple sexual partners or those co-infected with HIV (Zhang *et al.*, 2023) ^[39]. The virus does not spread through casual touch, and ordinary activities like hugging or exchanging utensils offer little risk (Liu *et al.*, 2022) ^[22]. Recent studies underscore the necessity for sustained attention in at-risk populations and enhanced screening measures to avoid transmission (Kramer *et al.*, 2023) ^[21].

Detection of HCV

Recently, a real-time RT-PCR analysis was successfully used for both basic research and clinical applications. (Heid *et al.*, 1996, Tyagi and Kramer, 1996) ^[15, 34]. Researchers from two groups described the use of real-time RT-PCR for quantification of HCV RNA (Kawai *et al.*, 1999, Martell *et al.*, 1999) ^[18, 23]. The real-time PCR approach addressed these issues by constantly tracking the PCR amplification process. The ability to monitor the amplification process in real time significantly enhances PCR-based DNA and RNA quantification. Real-time RT-PCR detects amplification of a PCR product during each cycling rather than the total

number of PCR products gathered at the conclusion of the PCR cycles. The release of a fluorescent reporter dye from a hybridizing probe in each cycle of real-time PCR is proportional to the amount of the PCR product (Heid *et al.*, 1996, Tyagi, 1996, Tyagi and Kramer, 1996) ^[15, 34]. The higher the starting copy numbers of the nucleic acid target, the sooner a significant increase in fluoresce is observed. The monitoring of the reaction in every PCR cycle. The higher the nucleic acid target's initial copy numbers, more quickly a significant increase in fluoresce is detected (Higuchi *et al.*, 1993) ^[16]. The monitoring of the reaction in each PCR cycle by the increment of emitted fluorescence rather than only the end product permits quantification of the early, exponential phase of reaction. As a result, multiple samples can be analysed at the same time. Furthermore, real-time PCR makes DNA and RNA quantification far more precise and reproducible because it uses threshold cycle (Ct) values calculated during the exponential phase of PCR rather than endpoints. In this latest paper, we disclose a highly specific, sensitive, and reproducible real-time RT-PCR approach using the specific primers and probe specified in the very conservative 5'-non-coding region (5'-NCR) of HCV genome that allows the quantitation of HCV RNA copies in human plasma and serum.

Polymerase Chain Reaction PCR and reverse transcription Polymerase Chain Reaction (RT-PCR) is an important technique in molecular biology for amplifying specific nucleic acid sequences. PCR is used to amplify DNA, allowing researchers to create millions of copies of a single DNA fragment. The technique requires multiple cycles of denaturation, annealing, and extension to promote the amplification of DNA sequences (Saiki *et al.*, 1985, Mullis & Faloona, 1987) ^[29, 27]. In contrast, RT-PCR is used to detect and quantify RNA. Reverse transcription converts RNA into complementary DNA (cDNA), which is then amplified using PCR methods. This approach is critical for diagnosing viral infections like COVID-19 and investigating gene expression (Nguyen & Patel, 2023) ^[21]. Both techniques are widely utilized in genetic research, clinical diagnostics, and forensic applications due to their high sensitivity and specificity.

Treatment of hepatitis C virus

The treatment of Hepatitis C Virus (HCV) has progressed substantially, notably with the development of Direct-Acting Antiviral (DAA) medications. These drugs target particular steps in the HCV life cycle and have been proven to achieve high rates of Sustained Virology Response (SVR), successfully treating the infection in most patients. Recent regimens, such as combinations of *sofosbuvir* and *velpatasvir* or *glecaprevir* and *pibrentasvir* offer shorter treatment durations, less side effects, and improved adherence over previous therapies (Zhang *et al.*, 2023) ^[40]. Despite these achievements, difficulties remain, including the high cost of DAAs, which can limit access to treatment, and the need for better screening and testing procedures to detect and treat infected persons early (Davis *et al.*, 2023) ^[12]. On-going research focuses on expanding global access to therapy and investigating possible vaccinations to prevent HCV infection (Houghton *et al.*, 2023) ^[17].

Recent treatments and researches of HCV

Recent research on the Hepatitis C Virus (HCV) has focused on a variety of topics, including advances in therapy, epidemiology, and vaccine development. Direct-Acting Antivirals (DAAs) have transformed HCV treatment, resulting in higher cure rates and fewer adverse effects than previous regimens. Recent trials have investigated the long-term efficacy of DAAs, showing Sustained Virology Response (SVR) rates of more than 95%, which reflecting a cure for the majority of patients. In addition, research has highlighted the need for more effective techniques to reach undiagnosed populations, particularly in low-resource settings, in order to meet the World Health Organization's objective of eliminating HCV by 2030. Epidemiological studies also show a changing demographic pattern for HCV infection, with an increase in frequency among younger groups,

Especially those who inject drug use Efforts to develop a vaccine are underway, with some promising candidates currently in early clinical trials. Yet, challenges remain to developing a universally effective vaccination due to the high variability of the virus (Cox & Page, 2021; Smith & Hagan, 2022; Grebely & Dore, 2023) ^[11, 31, 14].

Conclusion

Hepatitis C is a major health concern worldwide, impacting millions of people and leading to serious liver issues, such as cirrhosis and liver cancer, if not treated for severe liver complications, including cirrhosis and liver cancer. The advent of Direct-Acting Antivirals (DAAs) has revolutionized treatment, achieving cure rates exceeding 90% and transforming the management of HCV. However, to meet the World Health Organization's goal of eliminating HCV by 2030, it is crucial to enhance screening and treatment accessibility, particularly in underserved populations. On-going research is vital not only for improving therapeutic strategies but also for developing effective vaccines to prevent HCV infection. Continued efforts in education, awareness, and innovative healthcare solutions will be essential in combating this virus and reducing its impact on public health.

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