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Hapten-Based Vaccination as an Innovative Therapeutic Approach for Drug Addiction

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ABSTRACT

Introduction: Addiction to drugs is a prevalent illness marked by relapses. The standard treatments offered are insufficient to control and effectively manage addiction. Vaccination against specific substances to limit their influence on the brain and its reward system offers hope for treating addiction and relapse.

The purpose of this article is to share information with researchers and clinicians about creating a vaccine by incorporating a specific substance of abuse in a hapten conjugate that triggers an immune response against the effect of the drug.

Conclusion: Using hapten-based vaccination to treat drug addiction is a novel approach worth investigating.

Keywords: Drug Addiction; Substance Misuse; Hapten; Vaccination

Introduction

Drug addiction is a huge public health issue all over the world. The frequency of serious drug addiction, such as opioid and cocaine addictions, varies by region and location, but it is a worldwide issue affecting millions of people and communities [1]. Treatment difficulties emerge because of the complexities of addiction and the sociocultural variables that contribute to its persistence. There is an on-going and growing collaborative effort to develop appropriate methods to restrict its contagiousness and to mitigate any direct and indirect harm [2]. Addiction is described as a "chronic relapsing disease", with extremely high relapse rates that range from 56.8% to 81.8% [3]. According to the United Nations Office on Drugs and Crime's (UNODC) World Drug Report 2021, an estimated 275 million people worldwide (5.5% of the global population aged 15-64 years) used drugs at least once in 2020 [4]. Opioids, which include both prescription opioids and criminal drugs like heroin, make for a large portion of drug use and addiction. . Although pharmacotherapies such as opioid agonists and antagonists have demonstrated some success in treating opioid addiction, they can be insufficient and typically result in significant relapse rates [5]. Due to the challenges facing opioid use disorder treatments, development of a vaccine against heroin has become a major research focus. Producing an efficient vaccine against heroin addiction has been particularly challenging because of the need to generate potent immune response against heroin as well as its multiple psychoactive metabolites [6].

Drugs with low molecular weight as antigens can bind to antibodies but are not immunogenic. An antigen is any substance, such as a molecule, moiety, foreign particulate matter, or allergy, that induces the immune system to create antibodies against it. All antigens are

recognized by antibodies, which are produced initially in response to the antigens [7]. However, only high molecular weight antigens, which are called immunogens, can stimulate immune responses [8]. Drugs of abuse can be considered as haptens. They are small molecules that become immunogenic only when they are combined with larger carrier proteins [9,10]. Landsteiner first coined the term "haptenic immune response" to assist generate the idea of detecting anti-hapten antibodies in immunodiagnostics and therapies [11]. This approach has recently been followed in the quest for finding innovative treatments such as inventing vaccines against infectious diseases [12], which is equally useful in the treatment of addictions and their relapse. From the chemical standpoint, the hapten is a low molecular weight chemical agent, that must bind to a large carrier protein to create a conjugate (Figure 1), before being detected by the immune system and eliciting an immunological response. However, from the cellular perspective, after binding of hapten to a carrier protein and formation of the complexes that are processed inside Antigen Presenting Cells (APCs) and presented as a stable hapten-peptide complex to the major histocompatibility complex class II (MHC II) settled in the tissues, an immune response will begin [13]. Hapten vaccines work by targeting the specific substance of abuse, such as opioids, cocaine, or nicotine, and triggering an immune response against it. The hapten molecule is chemically modifying the addictive substance to make it immunogenic. This modification typically involves attaching the hapten to a larger carrier protein or molecule, enhancing its immunologic reaction capability and later the hapten-carrier molecule is administered as a vaccine. Once inside the body, the immune system recognizes the hapten-peptide complex as a foreign substance and mounts an immune response against it.

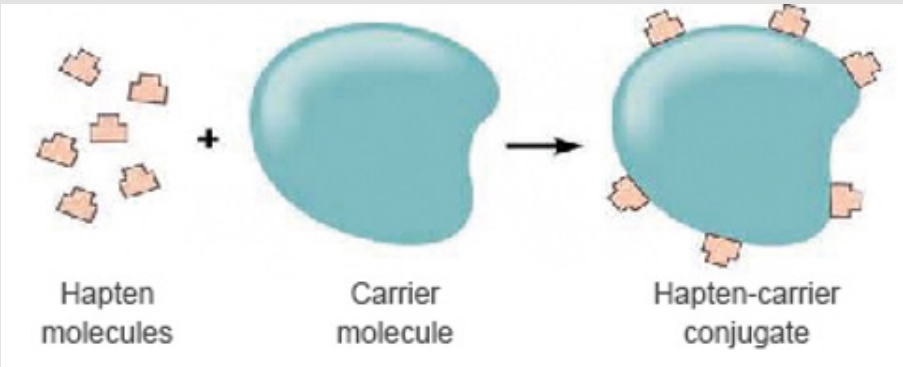

Figure 1: Hapten and carrier conjugation.

This immune response includes the production of antibodies that specifically bind to the hapten-complex. These antibodies produced in response to the hapten-complex vaccine circulate in the bloodstream. When a person subsequently uses the addictive substance, the antibodies bind to it, forming antibody-drug complexes. The formation of antibody-drug complexes prevents the addictive substance from reaching its target sites in the brain, thereby reducing the drug in the bloodstream and prevents it from crossing the blood-brain barrier. Hence, it will decrease the motivation to use the drug and potentially aid in overcoming addiction. One example of this hapten based vaccine is developing a method for conjugation of a morphine-like hapten (MorHap) to tetanus toxoid (TT). This includes conjugation of MorHap to the surface lysines of TT through the N-hydroxysuccinimide and the subsequent attachment of the thiol on MorHap to the maleimide portion of the cross-linker and increase its molecular weight to result in immune reaction against heroin [14].

Conclusion

Developing unique and innovative approaches to combating the ever-increasing incidence and hazards of addiction deserves urgent consideration. Therefore, hapten based vaccines are worth considering and developing.

Authors conflict

On behalf of all authors, we confirm that there is no any economic interest or any conflict of interest in this manuscript.

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