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OPINION

Improvement of opioid addiction medication through extended-release naltrexone: a comparative, experimental, and laboratory approach

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Numerous health and social relationship problems, namely an increased risk of contracting HIV, mortality, crime, unemployment and impaired interpersonal relationships, are related to drug dependence, with opioids at the helm. For this reason, opioid addiction is considered a major public health problem [1] and is characterized as a 'chronic relapsing disease' and is a major concern for public health, as are drug and alcohol addictions [1, 2]. In addition to social support and psychotherapy, treatment of opioid dependence relies on medication intake. The three main opioid-dependence treatment categories include opioid agonists, opioid antagonists, and non-opioid medications. Naltrexone hydrochloride (API), one of the most commonly used medications relies on an opioid antagonist. It reduces opioid cravings; it can be administered outside the hospital setting and cannot be abused [3]. However, during treatment several patients often forget to take a dose, doubling the next dose to compensate. In some cases, this finding in the therapeutic levels is not being reached, while in other cases undesired (side) effects appear. For this reason, especially in the case of long-term treatments of numerous diseases, an extended dosing interval is recommended, so that the patient receives the drug, only once a day, instead of two or three times a day. Extended-release drug delivery systems can lead to drug plasma concentrations remaining within the therapeutic range for longer, reducing adverse effects and increasing patient compliance [4]. Existing studies have shown encouraging results and especially from alternative administrations, including extended release, achieving an increase in duration of action and better compliance, due to less frequent administration [5]. Thus, it is considered appropriate to further investigate whether the extended-release opioid addiction treatment approach, can be applied to naltrexone, which is one of the most common medications, and in which way to best serve the patients' health and way of life. API has been selected for investigation, given that naltrexone can be administered per os for prolonged therapeutic effects [6]. The present study is in line with existing research [7-9] and compares the various extended-release forms of naltrexone tablets with the aim of finding the most suitable for release in the gastrointestinal tract. For this purpose, the tablets are prepared with three different excipients, namely inert substances included in the tablets in addition to the pharmaceutical substance. Excipients provide active ingredients with the desired properties and therefore formulate the drug by significantly influencing its quality and characteristics. The excipients used in this study are polyox or polyethylene oxide (PEO), Eudragit or polymethacrylate-based copolymers and magnesium stearate. This supports that the appropriate excipients are chosen for extended/modified release within a predetermined period of time depending on the objective of the dosage

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form design and the desired way of releasing the active ingredient. In particular, the comparative experimental laboratory study of the three excipients demonstrates that, in terms of their ability to extend the release of naltrexone hydrochloride, the absence of the Eudragit leads to a faster release of the active substance. Furthermore, when the Polyox and Eudragit ratios are varied, with the Eudragit L 100-55 ratio increasing, the release of the active substance is delayed. This article is a part of a collective laboratory research carried out as part of a degree thesis [10], which studied the release of the API, in two dissolution media of pH 1.2 and 6.8, respectively, by way of designing suitable controlled-release hydrophilic polymer matrix systems. This study focuses on the analysis of the pharmaceutical excipients. For the preparation of API's calibration curve two stock solutions of API have been prepared: (Cmax (NTX) = 0.26 mg/mL) in pH 1.2 and 6.8. Standard solutions have been prepared and measurements of their absorption have been effected following the technique UV-Vis. Preparation of tablets of a diameter of 10 mm, with three different recipes with varying quantities of ingredients. The data follows a normal distribution, and therefore, a statistical analysis was carried out using the t-test and ANOVA tests. Critical quality controls were carried out during the manufacturing of the tablets, and on the finished tablets. It was verified from these controls that the properties and characteristics of the tablets meet the necessary specifications. The tests conducted include the uniformity of weight, the uniformity of thickness, the hardness measurement, and the friability of the tablets. Based on these findings, it was verified that the tablets meet the Hellenic Pharmacopoeia specifications. Active pharmaceutical ingredient (API) acts by antagonizing opiate receptors with a high affinity for μ receptors, with remarkable therapeutic results for opioid and alcohol use dependence and addiction. Extended-release tablets were manufactured to study their release from specific drug delivery systems. Modified release tablets of the API were prepared and its modified release, from hydrophilic polymeric matrices, was studied. The results, which were obtained from this study suggest that the use of different excipients and combinations of them have a significant effect on the release of API. In particular, the absence of the excipient Eudragit L 100-55 brings about a more rapid release of the active substance from the tablets. Moreover, when the relevant ratios of Polyox (7x106) and Eudragit L 100-55 varied, with the amount of Eudragit L 100-55 increasing, the release of the API was retarded. API has significant clinical effects on opioid and alcohol dependence. It is also used effectively as an anti-inflammatory treatment for chronic pain, in low dosages, and dermatological diseases. Future research can therefore further possible additions to pharmaceutical treatments that can eventually also address withdrawal symptoms, such as anxiety and sleep disorders. Future studies can also investigate further new user-friendly methods of pharmaceutics administration, including percutaneous absorption and further extended-release [11]. Contributing towards dealing with the health and social plague of opioid addiction, and especially for the extended release of opioid addiction treatments, namely naltrexone, which is one of the most widely used medications, this study manufactured tablets to study the modified release of Naltrexone hydrochloride (API), aimed at finding suitable excipients for its release into the gastrointestinal tract, i.e., of pH 1.2 and 6.8, respectively. In conclusion, the classification of excipients, in terms of their ability to extend the release of naltrexone hydrochloride, is Polyox (7x106) < Eudragit L100-55. This study contributes to the design of dosage forms to achieve the desired mode of release of the active ingredient, by choosing the appropriate excipients, which allow the extended/modified release within a predetermined period of time and consequently facilitate the pharmaceutical treatment of patients.

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