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Enhancing Dissolution Rates in Fast-Dissolving Tablets of Antiemetic Agents: Formulation Strategies

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Abstract

The formulation strategies for enhancing the dissolution rates of fast-dissolving antiemetic tablets are studied, particularly with respect to Ondansetron. This is because, despite its wide application as an antiemetic drug, it has poor aqueous solubility and hence suboptimal bioavailability. Thus, a comprehensive approach has been adopted in which various excipients, namely superdisintegrants (Sodium starch glycolate, Crosscarmellose sodium), solubilizers (Poloxamer 188, Tween 80), and binders (Hydroxypropyl methylcellulose, Polyvinyl pyrrolidone) have been employed to optimize the formulation. The formulation of fast-dissolving tablets was based on a 2^2 factorial design, evaluating the effects of superdisintegrant and solubilizer concentrations on the dissolution rate of Ondansetron and prepared using the direct compression method. The characterization for the tablets was done by weight variation, hardness, friability, disintegration time, and dissolution study. SSG content with 6% and Poloxamer at 3% in optimal formulation F4 showed a 30 seconds rapid disintegration time along with tremendous increase in dissolution rates. Stability studies were carried out in accordance with the guidelines issued by ICH for three months on the formulations to confirm their physical integrity and drug content. The results indicate that the strategic selection and optimization of excipients play a very important role in tailoring the dissolution profiles of fast-dissolving Ondansetron tablets, thus therapeutic efficacy and time-to-relief against nausea and vomiting. It indeed provides a basis for further developments of fast-dissolving formulations of antiemetic drugs including better compliance of the patient with enhanced clinical results.

Keywords: Fast-Dissolving Tablets, Ondansetron, Antiemetic Agents, Super Disintegrants, Solubilizers, Dissolution Rate, Formulation Optimization

1. INTRODUCTION

FDTs have rapidly become popular in the pharmaceutical industry because of unique advantages over traditional dosage forms especially the enhancement of compliance by patients, hence, fast-dissolving tablets that dissolve almost immediately in the oral cavity without requiring water to dissolve; this makes it essential for populations suffering from difficulties in swallowing, such as pediatric and geriatric patients. The high priority is for fast-dissolving tablets of antiemetic agents for the treatment of special cases of nausea and vomiting because of chemotherapy, motion sickness, and postoperative recovery: due to a great number of patients suffering from these conditions. FDT formation with rapid onset action would enhance therapeutic outcomes and patient satisfaction.

The dissolution rate of the API is an essential factor that impacts the bioavailability and therapeutic efficacy of the drug. In case of antiemetic agents, rapid dissolution is crucial to address symptoms at an appropriate time. Unfortunately, most antiemetic drugs are beset by serious challenges, with several having poor solubility and stability as inherent physicochemical properties. Therefore, discovery of such efficient strategies that will increase the dissolution rates of such agents is of great importance. Formulation strategies in use of appropriate excipients, manufacturing techniques, and incorporation of innovative drug delivery systems are known to influence the dissolution profile as well as final performance of fast-dissolving tablets.

Amongst various strategies employed for enhancing dissolution rates, choice of excipient seems key. Superdisintegrants, for instance, are added to enhance the rate of disintegration followed by dissolution of the tablets when exposed to saliva. These excipients improve the disintegration of the matrix system so that the drug is exposed to the dissolution fluid more rapidly. Solubilizing agents as well as pH modifiers can be used to enhance solubility in cases

where drugs have antiemetic poor water-solubility levels. Scientists in the field of formulation have started looking at new innovative materials like nanocrystals and amorphous solid dispersions, which improve the solubility and rate of dissolution of a drug.

In fast-dissolving tablets formulation, direct compression, spray drying, and freeze-drying may be used for further optimization of the end dosage form. These approaches can significantly alter the particle size, porosity, and surface area-the parameters most critical for increasing the dissolution rates. Furthermore, advanced drug delivery devices, such as mucoadhesive polymers and lipid-based formulations, can also be included in FDTs to enhance the release profiles of antiemetic drugs.

2. REVIEW OF LITREATURE

Aapro et a (2021). conducted an extensive analysis of real-world prescribing data to review patterns of practice regarding the prophylaxis of CINV and adherence to guidelines of antiemetics. Their result highlighted discrepancies in guideline adherence and emphasized the call for optimization of antiemetic regimens in the name of maximizing patient outcomes. The topic of this article hints that healthcare providers should remain abreast of current guidelines and implement evidence-based practices within clinical settings as a way of guaranteeing the effective management of CINV.

Formulation of fast-dissolving tablets could probably be considered one of the most promising approaches toward enhancing poor-solubility drugs' bioavailability. Abd Elbary et al. demonstrated work on the preparation and in vitro evaluation of fast-dissolving tablets which contained a poorly soluble antipsychotic drug (2015). This study demonstrated that specific formulation approaches, such as addition of a superdisintegrant as well as taste-masked treatments, significantly improved tablet dissolution kinetics and patient acceptability. This work forms the basis for fast-dissolving formulations and would help in further development of the same to enhance therapeutic efficacy and facilitate patient compliance.

Abdulqader and Al-Khedairy (2017) was focused on the preparation and evaluation of taste-masked hydrochloride fast-dissolving tablets of ondansetron through techniques of solid dispersions. The results of their study showed that the taste of ondansetron could be masked effectively along with an improvement in the dissolution profile by solid dispersion. Such a study holds specific relevance to pediatric samples; the taste is one the factors determining compliance medication. As such, the successful application of the new technology of solid dispersion to their study supports the notion that this technology consists of unique properties that offer unparalleled potential to enhance the palatability and effectiveness of fast-dissolving antiemetic tablets.

Abhijeet (2022) presented an overview of fast-dissolving oral films. All the advances done in the past decade regarding fast-dissolving oral films have been put together here, and emphasis has been made on how new vehicles in the pharmaceutical world could substitute old tablet formulation 10 Advantages of these films are rapid disintegration, ease of administration, and improved patient compliance, especially among pediatric and geriatric populations. This review provides insights into the formulation strategies and materials used in the development of fast dissolving oral films. It opens avenues for further development of this novel drug delivery system in multiple therapeutic areas.

In the most recent review by Ahuja in 2015, a comprehensive review was conducted on the co-processing of excipients for fast-dissolving tablets, where the selection of excipients improves drug delivery systems. Here, the review will be focused on various co-processed excipients and their ability to modify different physical properties of fast-dissolving tablets, including flowability, compressibility, and disintegration time. The findings of Ahuja work to re-emphasize the need for further research in the development of excipients to meet specific demands posed by fast-dissolving formulations, which in turn could potentially better enhance dissolution rates and overall therapeutic efficacy.

3. MATERIAL AND METHOD

3.1Materials

3.1.1API

The antiemetic drug for this study is chosen to be Ondansetron, which has poor aqueous solubility, hence resultant poor bioavailability.

3.1.2 Excipients

Superdisintegrants: Sodium starch glycolate (SSG), Crosscarmellose sodium (CCS), and Microcrystalline cellulose (MCC).
Binders: Hydroxypropyl methylcellulose (HPMC) and Polyvinyl pyrrolidone (PVP).
Solubilizers: Poloxamer 188 and Tween 80.
Flavoring Agents: Natural and artificial flavors to make it more palatable.
Other Excipients: Magnesium stearate (lubricant) and lactose (filler).

Solvents

Various formulation techniques used the diluted water and ethanol.

3.1.3 Instrumentation

Tablet Compression Machine: These machines made use of compression in the direct compression process to compress the tablets.
Dissolution Tester: The paddle method apparatus USP Type II was employed for testing dissolution studies.
Sieve Shaker: This was used to find particle size distribution.
UV-Visible Spectrophotometer: This determined the concentration of the drug in dissolution samples**.**

3.2 Methodology

3.2.1 Formulation Development

Fast dissolving tablets were prepared using the direct compression method. Formulations were developed based on a 2^2 factorial design to investigate the effects of two independent variables: superdisintegrant concentration and solubilizer concentration on the Ondansetron dissolution rate.
Preparation of Blends: The API and the excipients were accurately weighed and blended for 15 minutes using a mortar and pestle to ensure uniform distribution of the excipients with the API.
Table Compress: The mixture was compressed into tablets using a tablet compression machine. Sufficient pressure was applied to get tablets, the hardness of which was around 3-4 kg/cm^2.

3.2.2 Characterization of Fast-dissolving tablets

Prepared fast-dissolving tablets were characterized for various parameters as discussed below:
Weight Variation: The average weight of 20 tablets was determined by using an analytical balance.
Hardness Test: The hardness of tablets was recorded with the help of a hardness tester.
Friability Test: The tablets were tested for friability in a friabilator. This should not exceed 1%.
Disintegration Time: The disintegration time was tested by using a disintegration tester in simulated saliva, pH 6.8.
Dissolution Study: The dissolution profile of the tablets was evaluated with the paddle method in 900 mL of dissolution medium, phosphate buffer pH 6.8, at 37°C, with samples taken at regular intervals and analyzed by UV-Visible spectrophotometry.

3.2.3 Stability Studies

As per ICH guidelines, stability studies were carried out. The formulations were placed under accelerated conditions at 40°C ± 2°C/75% ± 5% RH for three months, and physical appearance was analyzed along with drug content and dissolution profile at various intervals.

4. RESULTS

4.1 Formulation Development and Characterization

4.1.1 Formulation Optimization

The formulation optimization led to the formation of several formulations with varying concentrations of superdisintegrants (SSG and CCS) and solubilizers (Poloxamer 188). The optimized formulations were named F1 to F5.

4.12 Physical Characteristics of Tablets

Weight Variation: All formulations exhibited acceptable weight variations, ranging between ±5% of the average weight and were compatible with the pharmacopoeial standards.

Hardness and Friability: Tablet hardness ranged from 3.0 to 4.5 kg/cm² thus excellent mechanical strength. The friability values were within the acceptable range ≤1%.

Disintegration Time: It was formulation dependent. F4 containing 6% SSG + 3% Poloxamer possessed the shortest disintegration time of 30 seconds, which is significantly lower than the control.

Table 1: Physical Characteristics of Fast-Dissolving Antiemetic Tablets

Formulation	Average Weight (mg)	Hardness (kg/cm²)	Disintegration Time (s)	Friability (%)
F1	150 ± 5	3.5 ± 0.2	75	0.52
F2	150 ± 5	3.7 ± 0.3	60	0.48
F3	150 ± 5	4.0 ± 0.2	45	0.35
F4	150 ± 5	4.2 ± 0.2	30	0.29
F5	150 ± 5	3.8 ± 0.3	50	0.41

4.1.3 Dissolution Studies

The release profile of the prepared tablets was studied. Significant improvements in the release of Ondansetron were found. Results are given in Table 2.

Table 2: In Vitro Dissolution Profiles of Fast-Dissolving Tablets

Time (min)	% Drug Released (F1)	% Drug Released (F2)	% Drug Released (F3)	% Drug Released (F4)	% Drug Released (F5)
5	45.2	52.3	60.1	75.8	68.4
10	75.4	80.5	85.2	92.4	88.7
15	89.7	91.2	94.5	98.5	95.4
30	95.4	94.7	96.3	99.2	98.0

Average weight: All preparations of an average weight of 150 mg should be crucial for maintaining uniformity in batches.

Hardness: The range of values for hardness varied from 3.5 to 4.2 kg/cm², indicating that all the formulations had quite sufficient strength in mechanical properties and could withstand the rigours of handling and transportation.

Disintegration Time: The F4 composition had the shortest disintegration time of 30 seconds, hence suggesting that it had a fastest rate of disintegration in the oral cavity.

Friability: The friability values of all the formulations were less than 1%. This means that there were no cases of chipping or cracking in the handling of the tablets.

5. DISCUSSION

The results of this study were that it showed prominent advancements in developing fast-dissolving tablets containing Ondansetron by systematic inclusion of superdisintegrants and solubilizers. More precisely, it has been illustrated that the use of Sodium Starch Glycolate (SSG) as a superdisintegrant would ensure rapid disintegration of the tablets upon contact with saliva. Thus, the best formulation was F4, which presented an impressive disintegration time of only 30 seconds and the highest rates of dissolution. Such a rate of degradation is critical for the quicker availability of the drug to be absorbed, especially in clinical cases where chemotherapy-induced nausea or postoperative vomiting are present and time is a concern. The role of Poloxamer 188, added as a solubilizer, significantly improved the solubility of Ondansetron, a practically athermally water-insoluble drug, to ensure that more

of the active ingredient was present in solution for faster absorption. This synergistic effect provides the reason to select excipients that could significantly enhance the final therapeutic efficacy of antielectic tablets. Optimizing the concentrations of the combination SSG and Poloxamer 188 in the formulations helped achieve this work, wherein careful formulation design can lead to improved physical characteristics such as hardness and friability, as well as pharmacokinetic properties. The consequence of increased dissolution rates is that the onset of drug action becomes accelerated. Even comfort of the patient is increased, but at the same time, compliance with treatment would be improved since a patient would favor formulations that provide a speedy relief of symptoms. It therefore gives very valuable insights as fast-dissolving tablets are developed to consider the need for more research in excipient interactions that affect drug release profiles to better improve patient outcomes in various settings.

6. CONCLUSION

The addition of superdisintegrant SSG and a solubilizer in the form of Poloxamer 188 has been essential in the designing of effective fast dissolving tablets of Ondansetron to give its extraordinary therapeutic superiority. The optimized formulation, F4, demonstrates how thought put in before designing any formulations might result in significant improvement in dissolution rates, which happens to be particularly required for rapid onset of action during cases of nausea and vomiting. Such formulations may, thus, rapidly provide relief to patients, which is very important in acute settings like postoperative care or chemotherapy by ensuring the tablet disintegrates rapidly and the active ingredient is well solubilized. Given the importance of excipients in tablet physical and pharmacokinetic properties, such a study provides an ideal point of departure for work in future fast-dissolving formulations. It establishes an example for future research and development in the field. The learning that may be derived from this study should allow for ongoing exploration of how excipient interactions affect the release profile of the drug and optimize therapeutic efficiency with improved patient compliance. By focusing on such aspects, the pharmaceutical field was able to act more innovatively and to improve patient outcomes in various clinical scenarios. With this, the important association of formulation strategies with proper healthcare delivery could be well demonstrated.

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