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Review Methods for Analyzing the Composition and Properties of Pharmaceutical Formulations of Tablets

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Abstract: *The development of medicine brought about a revolution in human health. These medicines work best only if they are free of impurities and taken in the right amount. Many drugs and devices are constantly being developed, which involves testing the drugs to ensure they work. Impurities will be introduced into these drugs at different stages of development, transportation and storage, making their management risky and must therefore be controlled and measured. Analytical tools and techniques play an important role in this. This review highlights the role of analytical tools and analytical methods in drug quality assessment. This review focuses on various analytical techniques such as titration, chromatography, spectroscopy, electrophoresis and electrochemistry and their relationships in drug analysis.*

Keywords: Analytical techniques , Titrimetry , Chromatography, Spectroscopy, Electrochemicalmethods..

I. INTRODUCTION

The development of medicine brought about a revolution in human health. These medicines work best only if they are free of impurities and taken in the right amount. Many drugs and devices are constantly being developed, which involves testing the drugs to ensure they work. Impurities will be introduced into these drugs at different stages of development, transportation and storage, making their management risky and must therefore be controlled and measured. Analytical tools and techniques play an important role in this. This review highlights the role of analytical tools and analytical methods in drug quality assessment. This review focuses on various analytical techniques such as titration, chromatography, spectrometry, electrophoresis and electrochemical techniques.

The popularity of near-infrared (near-IR) spectroscopy is rapidly increasing for many reasons. Availability of inexpensive yet powerful computers and chemometric software for spectral data analysis is fostering the growth of new applications of the technique. The development of rapid-scanning spectrometers offering very high signal-to-noise ratios, an increased understanding and acceptance of the method in a variety of industries, and the need to maintain real-time process control in an era of total quality management are other reasons this method has begun to receive such attention. Near-IR spectroscopy has been used for a wide range of analyses in industries as diverse as biomedicine and petrochemicals.

Although the pharmaceutical industry has been relatively slow to embrace this technique, a variety of pharmaceutical applications of near-IR have been identified and investigated. This review will discuss the development of near-IR spectroscopy for the analysis of pharmaceutical dosage forms, specifically solid dosage from matrices, capsules, and tablets. The chemometric techniques used extensively in these analyses will also be discussed briefly.

Material

Potassium citrate (monohydrate), sodium bicarbonate, citric acid (monohydrate), tartaric acid, PEG 6000, sodium benzoate, manitol, sorbitol and aspartame were procured by Merck (Darmstadt, Germany). Povidon k-30 (PVP) was purchased from Rahavard Tamin (Tehran, Iran). Orange flavoring agent was procured from Kagawa (China) and raspberry, strawberry, cherry and lemon flavoring agents were prepared by Farabi pharmaceutical Company, (Isfahan, Iran).

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Preformulation

Firstly, the formulas were made up in the different stoichiometric ratios from tartaric acid, citric acid and sodium bicarbonate based on below reactions.

According to , materials of each formulation were weighed and then 2700 mg of monohydrate potassium citrate was added to each formulation. Finally, after preparation of appropriate mixture, the lubricants including 30 mg of PEG 6000 and 10 mg of sodium benzoate were added the mixture and then the tablets compressed by using a single-punch press machine (KILIAN & CO, Germany). For next stages, the better stoichiometric ratios were selectedwith regard to three factors: solubility, effervescence time and pH.

Methods

The coating also provides physical protection and resistance to chemicals; It also changes the release behavior of the drug. In the 19th century, modern chemical coating, namely sugar coating, began to be used to cover the bitter taste. Sugar coating has some disadvantages or limitations; long working time, about 6 to 7 days; and requires multi-step work (sealing, priming, trimming, coloring, polishing, etc.) for a skilled worker. Additionally, there are problems such as lack of automation in the coating process, increased weight, and preference for sugar solutions to harbor bacteria, which leads to the discovery of other layering processes. Film coating greatly reduces the processing time of sugar coating. In 1954, Abbott Laboratories introduced the first film- coated tablet. Among the coating methods, the fastest changing is film coating; ensures consistency in design from batch to batch; It can be used in many forms and can easily understand the process control and automation process. Water-based and organic-based polymersolutions can be easily used in the film process, but both polymer solutions have disadvantages. The organic solvent used for film coating has disadvantages such as flammability, toxicity, leaving heavy residue on the film, and the high cost of the organic solvent. In aqueous film coatings, the increase in required heat and drying time significantly increases the total production cost and constitutes a major disadvantage [2]. Compression coating technology was first introduced by Noyes in a patent in 1896. In the development of new drug delivery systems,the compression layer is one of the best options and a new layer. It is used in pharmaceuticals forvarious purposes such as structural release, pulsatile release, specific release in the intestine and systemic release. According to many available documents, compression coating technology is used to produce tablets such as compression coated tablets, such as the development of glipizidetablets aimed at achieving zero-order release [6]. To overcome film or sugar layer problems, tablet-in-tablet or compression layering has been introduced to replace the layering process. It is also called dry plating or plating and was one of the first non-toxic methods. Generally speaking,a tablet in tablet or compression coated tablet consists of two parts; one is the core and the other is the outer shell. The coating layer surrounds the core and generally controls the strength, drug release and stability of the film coating

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Advantages of tablets in tablet systems

Separation of different data can be done in the core and shell. Can be used to develop released products (such as delayed-release products) A tablet within a tablet consisting of two different drugs can target two different areas of the intestine. A layer layer for the tablet can be avoided during the layering process between the tablet core and the layer. It is a solvent-free coating andtherefore environmentally friendly. In tablet dosage forms, pharmacokinetic (drug-to-drug) interactions of concomitantly administered drugs can be avoided by establishing a time for drug release. Tablets in tablet dosage forms provide protection for hygroscopic or thermostable drugs. A tablet in tablet dosage form that can act immediately and stimulate the release of similar drugs or combinations of different drugs.

Challenges related to Tablet in Tablet technology

The cross contamination possibility between the layers. Between the adjacent layers, the elasticmodulus is a mismatch. There are an inadequate layer attachment and relatively low interfacial strength because of the high elastic modulus ratio between neighboring layers. Face challenges for long term retaining physical and chemical integrity of device during its storage. Due to the large tablet size, it creates a swallowing problem . Different layers when the main tablet is not in the middle of the system

The coating also provides physical and chemical protection; It also changes the release behaviorof the drug. In the 19th century, a traditional coating known as sugar coating was used to mask the bitter taste. Icing has some disadvantages or limitations; long working time, about 6 to 7 days; and needs to be processed by skilled workers in several stages (sealing, priming, trimming,coloring, polishing, etc.). In addition, there are problems such as the lack of automation in the coating process, the increase in weight, and the tendency of sugar to hide bacteria, which leads to the discovery of other methods layer by layer. Film coating greatly shortens the sugar coating process time. In 1954, Abbott Laboratories introduced the first film-coated tablets. The fastest changing coating method is film coating; ensuring product consistency from batch to batch; It can be used in many ways and allows easy understanding of control processes and automation processes. Water-based and organic-based polymer solutions can be easily used in the thin film process, but both polymer solutions have disadvantages. Organic solvents used for film coating have disadvantages such as being flammable, toxic, leaving more film and being more expensive. Increasing the need for heating and drying time in aqueous film coating increases the overall production cost and causes a decrease in performance. Compression layer technology was first introduced in a patent by Noyes in 1896. In the development of new drug delivery systems, compression layer is one of the best choices and new methods. It is used in medicine for various purposes such as release, pulsatile release, intestinal-specific release and systemic release. According to many available documents, compression coating technology is used to produce tablets such as compression coated tablets; for example, glipizide tablets are designed toprovide zero-order release . To overcome the problem of film or sugar coating, layering has beenreplaced by chip-in-chip or compression layering. It is also called dry plating or electroplating and is one of the first non-toxic processes. Generally, tablets or compressed tablets consist of twoparts; a core and a shell. The outer layer surrounds the core and generally controls the strength, chemical release and stability of the film layer .

Advantages of tablet computers in tablet computer systems

Separation of different information can be done in the core and shell. It can be used to create product releases (such as soft-release products). The tablets inside the tablet contain two differentmedications that can target two different parts of the intestine. Coating of the tablet can be prevented during delamination of the cores and coating. It is non-toxic and therefore environmentally friendly. In tablet dosage forms, pharmacokinetic (drug-drug) interactions of co-administered drugs can be prevented by time release. Tablets in tablet dosage forms provide protection for hygroscopic or heat-stable drugs. Tablets in tablet dosages that act immediately and stimulate the release of similar drugs or different drug combinations.

Problems with tablets in tablet technology

There is a possibility of contamination between layers. The elastic modulus of the layers is not uniform. Due to the high elastic modulus ratio of the layers, the adhesion layer is insufficient andthe interface strength is low. Face the challenge of maintaining the physical and chemical integrity of the device for long periods of time during storage.

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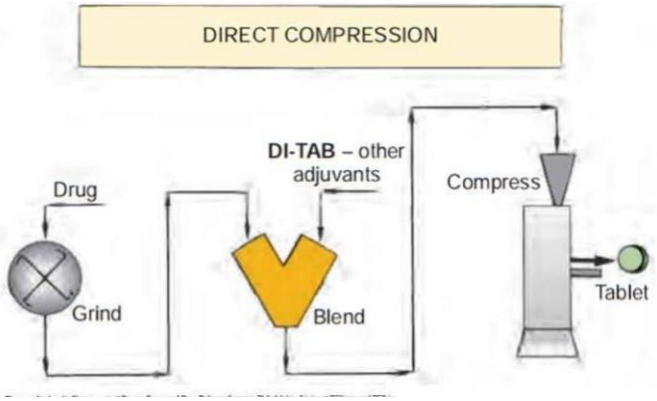
Example

Methods of Potassium Citrate Effervescent Tablets Production

Direct Compression :- According to , raw materials of each formulation were weighed and weremixed in a tumbling cubic blender for 15 minutes. After the preparation of the primary powder mixtures, sweeteners including aspartame, sorbitol, mannitol and fruit flavoring agents were passed through the appropriate mesh and were added to the powders and these were mixed altogether for 5 minutes. Finally,the selective lubricants including sodium benzoate (10 mg) and PEG 6000 (30 mg) were added and again mixed for about 2-5 minutes with other material.



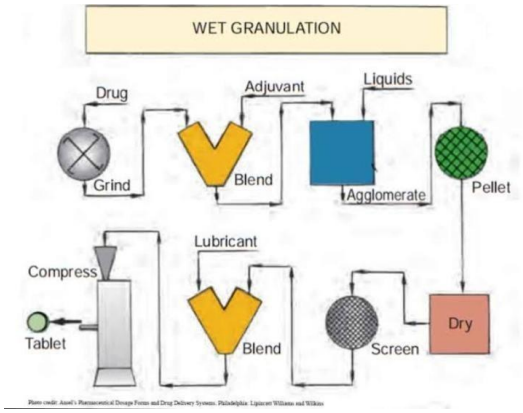
Then, the powders were compressed into tablets by using a single-punch press machine (KILIAN & CO, Germany), with 25 mm punch set. Weight ofeach tablet was considered about 4.5 g. At the end, the tablets were dried in an oven with air circulation at 54°C for 1 hr and after cooling were packed inplastic tubes.

Fusion Method

According to the formulations which are shown in amounts of citric acid, sodium bicarbonate, potassium citrate and mannitol (sorbitol) were weightedaccurately and were mixed for about 15 minutes in a tumbling cubic blender.Then, the obtained mixture was placed in an oven at 54 °C. The powder wasmixed regularly until the crystallization water of citric acid was released as binder factor (approximately 30 minutes). After obtaining an appropriate pasty mass, this wet mass was passed through sieve No. 20 and the obtained granules were dried in an oven at 54 °C for 1 hr. After drying, for second times the granules were passed through sieve No. 20.

In the next stage, sweeteners and flavors were added with the granule massand mixed for 5 minutes with other material. At last, the lubricants including sodium benzoate (10 mg) and polyethyleneglycol 6000 (30 mg) were added and mixed for 2-5 minutes with other material. The granule mixtures compressed into tablets by a single-punch press machine (KILIAN & CO, Germany), with 25 mm punch set. Finally,they were dried and packed with the previous methods

Wet granulation Method



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Wet granulation was performed on F5 and F6 formulations. First, citric acid and sodium bicarbonate and potassium citrate were milled by using miller so that all powders were passed through sieve No. 35 and were blended for 10 minutes. Then 9.5 % w/v PVP solution in absolute ethanol was added with the mixture, so that white pasty mass was formed. This wet mass was passedthrough sieve No. 20 and the granules were dried in an oven at 54 °C for 75 minutes. So, the dried mass was passed through sieve No. 20 and the other ingredients were added to them like as fusion method. The granule mixtures were compressed into tablets by using a single-punch press machine (KILIAN & CO, Germany), with 25 mm punch set. Prepared tablets were dried in an oven with air circulation at 54 ° C for 90 minutes, then were wrapped in Aluminum foil and were packaged in plastic tubes.

Precompression Tests

Particle Size Analysis

The average particle size of powder mixture was determined by sieve analysis method. 100 grams of powder mixtures and granules poured on the upper sieve. Series of sieve were placed on ERWEKA shaking apparatus for10 minutes after this period; the amount remaining on each sieve was measured.

There are several reasons why defects can occur during formulations,including:

- Inaccurate measurements: If the ingredients are not measured correctly, it can lead to an imbalance in the formulation, resulting in defects.
- Poor ingredient quality: Using low-quality or expired ingredients can lead to defects in theformulation.
- Incompatibility of ingredients: Some ingredients may not be compatible with each other,leading to defects in the formulation.
- Incorrect mixing or blending: Improper mixing or blending of ingredients can result in defects in the final formulation.
- Environmental factors: Factors such as temperature, humidity, and air quality can also impactthe formulation process and lead to defects.
- Contamination: Contamination from external sources can also lead to defects in theformulation.

To prevent defects during formulations, it is important to carefully measure and select high- quality ingredients, ensure compatibility of ingredients, follow proper mixing and blending procedures, and maintain a clean and controlled environment during the formulation process. Regular testing and quality control measures can also help identify and address any defects in theformulation.

II. CONCLUSION

In this work, it was tried to produce potassium citrate effervescent tablets byusing direct compression, fusion and wet granulation techniques. The results of this study show that wet granulation is a suitable method to produce effervescent tablets of potassium citrate due to the large size of these tablets in the pharmaceutical industry. Wet granulation is one of the most common methods used for granulation in the industry. This method is obtained by adding a solution with (or without) adhesive to the powder to form a wet mass. In this study, the prepared tablets were acceptable under the terms of pharmacopoeia standards only when PVP was added as a binder during the granulation process.

Due to particle adhesion, the prepared tablets through wet granulation technique had better compression and uniformity. They had not processing problems such as sticking, capping, and friction.

Among the studied formulations, only the formulation G6 was desirable for all physiochemical characteristics, including effervescent time under 3 minutes or less, pH <6, friability under 1 percentage, the water content below 0.5 percentage, low weight variation, and correct content uniformity. Finally, its taste was also amended by adding strawberry - raspberry flavor.

These tablets will help to convenience consumption of potassium citrate and more acceptances of patients who are affected by urate and calcium kidney stones.

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