تفريغ لاب صناعية

المحاضرة: Exp. 6

الصيدلاني/لة: أديج خولاز

Soul Academy

لجان الدفعات

Experiment No. 6

Effervescent Granules

Objectives:

1. To prepare effervescent Granules using wet method.
2. To evaluate the prepared effervescent granules.

The effervescent forms are defined within Pharmacopeias as "those granules or tablets to be dissolved in water before administration to patients." They are used to administer water-soluble active ingredients, especially when the large dosage is required.

Effervescent granules are dosage form composed of dry aggregates powder particle; containing a medicinal agent in a dry mixture usually composed of sodium bicarbonate, citric acid, and tartaric acid when added to water, the acids and the base react to liberate carbon dioxide, resulting in effervescence. The resulting carbonated solution masks undesirable taste of any medicinal agent.

Effervescent dosage forms also enhance patient compliance. They are easier to administer, particularly helpful to patients, like children, who are not able to swallow capsules or tablets. A pleasant taste, because of carbonation, helps to mask the bad taste of certain drugs. This could also help to avoid the gastric side effect of certain drugs .They are easy to use and appeal to consumers for color and fizzy appearance more than traditional dosage forms.

Effervescent granules are having: high solubility, high stability, fast dissolving property and are also convenient dosage forms. Just before administration these granules are to be mixed in a glass of water and this solution or dispersion should be immediately drunk. The granules are quickly dispersed by the evolution of Carbon dioxide in water due to interaction between acid and base in the presence of water. Due to the liberation of Carbon dioxide gas, we observe the

dissolution of the active pharmaceutical ingredients in water as well as taste masking effect is also enhanced.

why do we use it?

ADVANTAGES

1. Easy to administer مجرد ما حطها في كأس الماء تصير جاهزة للشرب
2. Easily portable and Marketing aspects.
3. Onset of action is faster Solution لأنها
4. Gentle on the digestive tract
5. It masks unpleasant taste also. Carbonation الـ → سبب → زي المشروبات الغازية
6. More stable than liquid dosage form

Stability أقل Liquids

Limitations of effervescent formulations why we don't use it in some cases?

1. It cannot be given to the children because of possibility of gas (CO2) toxicity. → ما يسبب نعطيها للأطفال عادتًا أقل من 12 سنة ليتوفر شكل آخر للأطفال
2. If packaging is not done properly then there are chances of degradation by environmental moisture. إذا كان التغليف غير مناسب رح تدخل عليه رطوبة ورح تخرب الـ Formula إذا انهار تفاعل بين الـ acid والـ Base.
3. It has shorter shelf life as compared to other solid dosage forms. ما تتحمل الحرارة والرطوبة ولا متطلبات التخزين الطويلة
4. It requires special machinery requirements for manufacturing. 5. This dosage form is costly then tablets. → (تحتاج عناية أكثر) ١- تحط مواد أكثر ٢- والتغليف لكل dose لحالها.

Preparation of Effervescent Granulation

النسبة | citric acid : tartaric acid | 1 : 2 |

It has been found that citric acid monohydrate and tartaric acid used in the ratio of 1:2, respectively, produces a powder with good effervescent properties. The amount of sodium bicarbonate to be used may be calculated from the reaction which occur when the granules come in contact with water.

رح نشوف تحت حسب المعادلات و كيف منوصل كمية الـ Sodium bicarbonate اللي نحتاجها.

MECHANISM OF EFFERVESCENCE

As we already know that Effervescent granules contain acid (citric acid) and base (Sodium bicarbonate) it rapidly reacts in water by releasing CO_2. Due to liberation in CO_2 gas, the active pharmaceutical ingredient (API) is dissolved in water as well as taste masking effect is enhanced. The reaction between the citric acid and Sodium bicarbonate it results in liberation of CO_2 shown as follows

$$C_6H_8O_7.\ H_2O + 3NaHCO_3\ (aq)\ Na_3C_6H_5O_7 + 4H_2O + 3CO_2\ (aq)$$

(Citric acid) (Sodium bicarbonate) (Sodium citrate) (Water) (Carbon dioxide)

acid + Base → الناتج يتفكك ويعطي CO_2

الناتج ⇒ Salt + Water + CO_2

$C_4H_6O_6 + 2NaHCO_3 \; Na_2C_4H_4O_6 + 2H_2O + 2CO_2$ (g)

(Tartaric acid) (Sodium bicarbonate) (Sodium carbonate) (water) (Carbon dioxide)

Method of preparation

Dry or Fusion Method

It is the most important method for the preparation of effervescent granules. In this method the powders are heated using an oven or source of heat. Fusion method uses the water of crystallization present in the citric acids which acts as binding agent. The powdered mixture is stirred well to obtain a uniform mass and is passed through a sieve to obtain granules and is finally dried in an oven

Wet Method

The wet granulation method is the most widely used method. This method firstly involves weighing, sifting of the ingredients using sieve , transferring the sifted material to Rapid Mixer, mixing it for five minutes at a slow speed and adding binder solution to it. Following this, the mass is passed through a sieve and dried at 50°C using tray dryer.

1. All ingredients are mixed thoroughly for uniform distribution

↓

2. Pass the powder through sieve to obtain uniform particle size

↓

3. Add suitable amount of binding agent

↓

4. Wet mass is passed through the sieve to obtain desired size granules

↓

5. These granules are dried in hot air oven.

E.G

EVALUATION OF EFFERVESCENT GRANULES

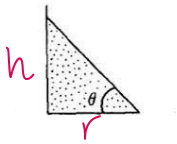
بعد ما حفظناهم وحصلنا على الـ E.G الموجودين حدنا خلينا نشوف شو هي الـ evaluations لـ E.G .. ما هي الفوائد اللي لازم اعملها مشان اختبر الـ E.G تاعتنا

1. Angle of repose

Using fixed funnel method, the angle of repose can be determined by passing the prepared granules in funnel. The measurement of height(h) and radius(r) of granule pile gives angle of repose which indicates the flow property of granules.

$\tan \theta = h/r$

$\Theta = \tan^{-1} (h/r)$



Where, h = Height of pile , r = Radius of pile

(نصف القطر)

2. Flow rate

Flow rate of granule has been defined as the rate at which the particular mass emerges through the orifice in funnel of suitable diameter. It can be determined by pouring the weighed quantity of granules in funnel with an orifice of 8mm diameter.

The time required for complete granule mass to emerge out of the orifice was recorded using a stopwatch. The flow rate was calculated from following formula,

$$\text{Flow rate} = \frac{\text{Weight of granules}}{\text{Time in seconds.}}$$

الوزن / الوقت اللي خلص معنا

3. Bulk density

In a measuring cylinder, a certain quantity of prepared granules were taken without compacting. The volume occupied by the granule is noted as V1 (bulk volume). Bulk density can be calculated by using the following formula,

$$\text{Bulk density} = \frac{\text{Weight of granules}}{\text{Bulk volume of granules}}$$

4. Tapped density

The volume occupied by the granule is noted as V2 (tapped volume). In a measuring cylinder, a certain quantity of prepared granules were taken and tappedfor 100 timesTapped density can be calculated by using the following formula,

اسطوانة, تم أخذ كمية معينة من الحبيبات المعدة والنقر عليها لمدة 100 مرة

$$\text{Tapped density} = \frac{\text{Weight of granules}}{\text{Tapped volume of granules.}}$$

EFFERVESCENT tablets هذا الـ test لـ

5. Carr's index

The percentage compressibility index of a granule was a direct measure of the potential strength and stability of granule. The Carr"s consolidation index can be calculated by using the following formula,

$$\text{Carr's index} = \frac{\text{(Tapped density – Bulk density)}}{\text{(Tapped density)}} \times 100.$$

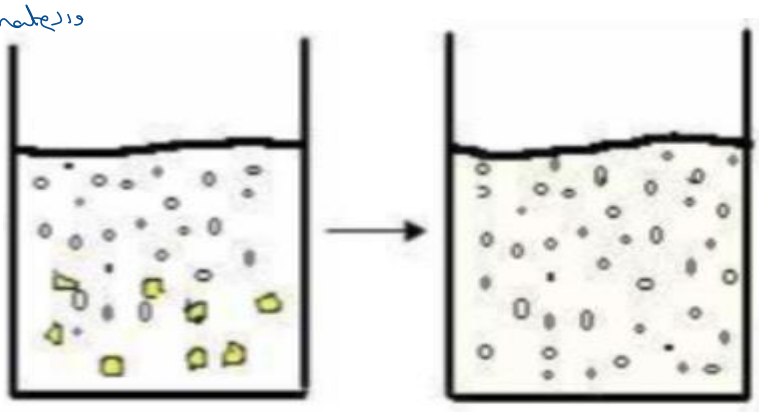
كل ما كان أعلى كل ما كانت قابليتها للـ compressibility تكون أعلى.

6. Effervescence time (water 50ml في Beaker ، يعني قد إيه الـ dose تحتوي يحطوها) عادةً one dose

In vitro effervescence time was measured by dissolving some quantity of granules in a beaker containing 50 ml of water. Granules were randomly selected from the batch. In vitro effervescence time was measured.

تفاعل بين الـ Citric acid و Sodium bicarbonate بوجود الـ Water وده بيطلع الـ bubbles الـ CO_2 gas. بسبب الـ

و لنحسب الوقت يلي صار فيه التفاعل.



7. Effervescence volume كم الحجم يلي وده يرتفع بعد الفوران

In vitro effervescence time was measured by dissolving some quantity of granules in a graduated cylinder containing 50 ml of water. Granules were randomly selected from the batch. In vitro effervescence volume was measured.

عشان نقيس ارتفاعه و نعرف الحجم تاعه

8. Disintegration test اختبار التفكك

حرارة الغرفة.

One dose of effervescent granules is poured in the beaker containing water at 15- 25°, numerous bubbles of gas is liberated. When the liberation of gas around the granules stop, granules get disintegrated, being either dissolved or dispersed in water. Repeat the operation on 5 other doses. يعني لازم نفحص 6 doses.

If each of 6 doses disintegrate within 5 minutes, then the preparation complies with this test.

Limit ← لازم يصيروا تفكك بني أقل من 5 minutes

9. Particle size by image analysis

Image analysis is a powerful analytical technique that provides particle shape information in addition to a sample's standard particle size distribution. This technique captures digital images of dispersed particles utilizing an appropriate objective/magnification and CCD camera.

Instrument software assigns a grey scale value to the pixels within the digital images and the operator evaluates the images to differentiate between particles and background. This process is known as "threshold" and based on the value set by the operator, the pixel is turned on or off. Each digital image is then processed by the software, and, once complete, results are available on a variety of size and shape parameters. Image analysis provides a very useful method for the measurement of the size distribution of granular materials. The method is very useful when the grains to be measured are very small (1 − 25 µm) .

يقوم برنامج الأدوات بتعيين قيمة مقياس رمادي للبكسلات داخل الصور الرقمية و

يقوم المشغل بتقييم الصور للتمييز بين الجسيمات والخلفية. هذه العملية

يعرف باسم "العتبة" واستنادا إلى القيمة التي حددها المشغل، يتم تشغيل البكسل أو

إيقاف. ثم تتم معالجة كل صورة رقمية بواسطة البرنامج، وبمجرد اكتمالها، تكون النتائج

متوفر على مجموعة متنوعة من معلمات الحجم والشكل. يوفر تحليل الصور طريقة مفيدة جدا

لقياس توزيع حجم المواد الحبيبية. الطريقة مفيدة جدا

عندما تكون الحبوب التي سيتم قياسها صغيرة جدا (1 - 25 ميكرومتر).

Experimental Part

Part 1 : Preparation of effervescent granules

Materials and instrument:

Master Formula:

(to prepare 20.0 g granules)

Material	Weight (g)
Magnesium sulfate	2.0 g
Citric acid monohydrate	2.8 g
Tartaric acid	5.6 g
Sodium bicarbonate	9.6 g

-Binder : Ethanol 96%

-Top loading balance

-Stainless steel Tray

-Sieve 1.4mm , 2.0 mm

-Drying oven

Preparation method:

1. Weigh the different ingredients based on the computed amount.
2. Using a mortar and pestle ; triturate the ingredients to ensure uniform and appropriate size for powder.
3. Transfer the powder
4. to a small tray.
5. Add a sufficient amount of ethanol 96% to make it wet.
6. Pass the mixture through sieve 1.4 mm or 2.0 mm.
7. Collect the wet granules in a suitable stainless steel tray.
8. Put in oven at 50 °C for 15 minutes.
9. After drying , collect the dry granules and pass through sieve used in step 5.
10. Evaluate the resulted granules as described in part 2.

Part 2 : Evaluation of effervescent granules

1. Effervescent volume:
   a. Put 50 ml of water in 100 ml graduated cylinder
   b. Weigh2.0 g of granules
   c. Add granules in cylinder containing water
   d. Measure the effervescent volume

2. Effervescent time and Disintegration time
   a. Put 50 ml of water in 100 ml beaker
   b. Weigh 2.0 g of granules
   c. Add granules in beaker containing water
   d. Measure the effervescent time
   e. After 5 minutes, the granules dissolve completely no any residue remaining in the beaker

3. Particle size analysis

   Refer to video to measure particle size of your granules

https://youtu.be/prQIZf5JajY?si=ExN98_8gQZO58AXv

* ما تنسوا تدعوا للمسلمين جميعًا

* ما تنسوا أهل الفاشر وأهل غزة و بورما

و إلا يخور ... استودعوا الله المسجد الأقصى دائمًا"

* ما تنسوا زميلنا أيهم من دعائكم ..

* دعواتكم بالبركة و التوفيق لو سمحتم ..

* إذا عندكم أي تعليم أو شيء تقبروا تتغير

بالتزيخ يا ربي تبعثوا لي Soul academy

Dreylamer