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SUITABILITY OF APPARATUS FOR DISSOLUTION STUDIES OF SALICYLIC ACID

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ABSTRACT
Dissolution testing plays an important role as a routine quality control test, for characterizing the quality of the product and plays a major role in drug development as it determines bioavailability and therapeutic efficacy. Dissolution of salicylic acid was carried out using various apparatus like the rotating basket, the rotating paddle, the rotating basket with paddle, the stationary basket-rotating paddle, and flow through cell system. The objective of this study was to study the suitability of apparatus for dissolution studies of salicylic acid. Salicylic acid compacts and capsules were prepared and dissolution studies were performed using USP type I and type II apparatus. The difference and similarity factors were calculated to compare the dissolution profiles of paddle and basket methods for both these dosage forms. The f_1 & f_2 values complied with the acceptance criteria, and no notable change was observed. Hence, the two apparatus may be interchangeable for carrying out the dissolution of salicylic acid.

KEYWORDS: Dissolution, Similarity factor, Difference factor.

INTRODUCTION

Dissolution is defined as the process by which a solid substance enters in the solvent to yield a solution. Stated simply, dissolution is the process by which a solid substance dissolves. Fundamentally, it is controlled by the affinity between the solid substance and the solvent.[1]

In the pharmaceutical industry, it may be defined as the amount of drug substance that goes into solution per unit time under standardized conditions of liquid/solid interface, temperature, and solvent composition.[2]

Dissolution testing is an official test used by pharmacopeias for evaluating drug release of solid and semisolid dosage forms. Dissolution tests were first developed to quantify the amount and extent of drug release from solid oral dosage forms including immediate/sustained-release tablets and capsules.[3]

It has been widely accepted that dissolution is the only batch release test that monitors the rate and extent of *in-vitro* drug release, and this test is often used as a surrogate to ensure consistent *in-vivo* performance. There are several ways in which dissolution testing plays a pivotal role in regulatory decision-making. It may be used to waive *in-vivo* bioequivalence (BE) study requirements, as BE documentation for Scale Up and Post Approval Changes (SUPAC), and to predict the potential for a modified-release (MR) drug product to dose-dump if co-administered with alcoholic beverages. Thus, *in-vitro* dissolution testing plays a major role in the FDA's efforts to reduce the regulatory burden and unnecessary human studies in generic drug development without sacrificing the quality of the drug products.[4]

Factors affecting dissolution

1. Physicochemical Properties of Drug
2. Drug Product Formulation Factors
3. Processing Factors
4. Factors Relating Dissolution Apparatus
5. Factors Relating Dissolution Test Parameters.[5]

Importance of USP Type I and II apparatus

The most used methods for evaluating dissolution first appeared in the 13th edition of the United States Pharmacopeia in early 1970. These methods are known as the USP basket (method I) and paddle (method II) methods and are referred to as "closed system" methods because a fixed volume of dissolution medium is used. In practice, a rotating basket or paddle provides a steady stirring motion in a large vessel with 500 to 1000 ml (about 33.81 oz) of fluid that is immersed in a temperature-controlled water bath.

The USP basket and paddle methods are the methods of choice for dissolution testing of immediate release oral solid dosage forms. The use of alternative dissolution methods should be considered only after USP methods I and II are found to be unsatisfactory.[6]

Importance of dissolution medium

Since the objective of drug dissolution testing is to assess the expected drug dissolution in the GI tract, the medium should be representative of the liquid-phase present in the tract, which is aqueous. Therefore, to be physiologically or bio-relevant, the dissolution medium

must be water or water-based. However, one may not use media such as potassium or sodium hydroxide solutions which, although water-based, their use is restricted by their high pH values not found in the GI tract. A general restriction imposed upon the choice of a dissolution medium by the physiological aspect is, therefore, that the medium be aqueous and have a pH in the range of 1 to 7. Furthermore, considering the physiological aspect with regard to dissolution testing, it is generally recognized that the most of time, if not always, absorption of drugs occurs in the intestinal part of the GI tract where the pH ranges from 5-7, and not in the gastric (stomach) section where the pH is usually 1 or sometimes 2-3.[7]

Dissolution of Salicylic acid

M. R. Baichwal et al (2008), evaluated four dissolution methods, the rotating basket, the rotating paddle, the rotating basket with paddle and the stationary basket-rotating paddle, using capsules and non-disintegrating pellets of salicylic acid. Stationary basket-rotating paddle method was found to offer several advantages over the rotating basket and rotating paddle method which have some limitations, which deserves serious consideration for adopting it as an official method for evaluating dissolution rates of various solid dosage forms.[8]

Riaz Uddin et al (2011), reviewed and focused on different mathematical aspects of dissolution process and different dissolution apparatuses are in use and also on modernization of dissolution process and dissolution testing apparatuses including automation in dissolution testing and adoption of fiber optic technology.[6]

Arulmozhi, A. et al (2011), investigated the dissolution performance of disintegrating Prednisone tablets and non-disintegrating salicylic acid tablets using the USP Dissolution Testing Apparatus 2. The study emphasizes the impact of tablet positioning within the apparatus on dissolution outcomes, highlighting that the dissolution performance of both disintegrating and non-disintegrating tablets is significantly influenced by their position in the USP Dissolution Testing Apparatus 2.[9]

Hight variability in dissolution testing outcomes suggests the need for careful selection of calibrator-apparatus combinations.

Significance of f_1 & f_2 Factor

A model-independent mathematical method was developed by Moore and Flanner (Moore and Flanner, 1996) for comparison of dissolution profiles using two factors, f_1 and f_2. The f_1 and f_2 factors provide a simple measure of similarity between pairs of dissolution profiles. The difference factor (f_1) is the percentage difference between two dissolution profiles at each time interval:

$$f1 = \frac{\sum \mathrm{Rt} - \mathrm{Tt}}{\sum \mathrm{Rt}} X\ 100$$

where, Rt indicates the released amount of drug of reference formulation; and Tt, the released amount of drug of test formulation. If the dissolution profiles are superimposed, $f1$ reaches a value of 0, whereas the factor value increases when the differences between dissolution profiles also increase. From a practical point of view, values of $f1$ between 0 and 15 can be considered as superimposed dissolution profiles. The similarity factor (f_2) can be calculated using the following expression:

$$f2 = 50 \times log\left[\left\{1 + \frac{1}{n} \times \Sigma(Rt - Tt)^2\right\}^{-0.5} \times 100\right]$$

where, N indicates the number of experimental data. Values of $f2$ between 50 and 100 can be considered as superimposed dissolution profiles.[10]

Table 1: Limits for similarity and difference factors.

Difference factor	Similarity Factor	Inference
0	100	Dissolution Profiles are similar
≤ 15	≥ 50	Similarity or equivalence of two profiles

MATERIALS AND METHODOLOGY

Preparation of Calibration Curve of Salicylic acid in Water

Preparation of 1% Ferric chloride solution in 1% Hydrochloric acid

A solution of ferric chloride was prepared by dissolving 1g of ferric chloride (anhydrous) (1% ferric chloride solution) in 100 ml of 1% v/v of hydrochloric acid (1 ml of concentrated hydrochloric acid in 100 ml of water).

Salicylic acid was dissolved in methanol, and various dilutions were taken and colored using 1 ml of 1% Ferric chloride solution in 1% HCl and the absorbance was measured using a colorimeter at 540 nm.

Procedure for preparation of Salicylic acid compacts & capsule

A saturated solution of salicylic acid was prepared using methanol by heating. The solution was cooled to get crystals. After the formation of crystals, the solution was filtered, and the product was dried.

The product was sieved and was compressed to compacts. 300 mg of salicylic acid was weighed and filled into capsules.

Procedure for Dissolution

Apparatus: USP type I & II apparatus.
Dissolution medium: Water

Rpm: 100
Temperature: 37± 0.5° C
Volume: 900 ml
Time: 75 minutes
900 ml of Distilled water was transferred to the dissolution vessel and 300 mg Salicylic acid capsule was placed and agitation was started.
At definite time intervals, 5 ml of sample was pipetted and replaced by 5 ml of distilled water.
The samples were analyzed using a colorimeter, by appropriate dilution, and the addition of 1 ml of 1% Ferric chloride solution to each was done and the absorbance was measured at 540 nm.

RESULTS AND DISCUSSION

Standard Graph

Dilutions of salicylic acid were prepared using water and were analyzed using colorimeter at 540 nm. The standard graph was plotted, where the concentration of salicylic acid was taken on the x-axis, and absorbance was taken on the y-axis as shown in figure 1.

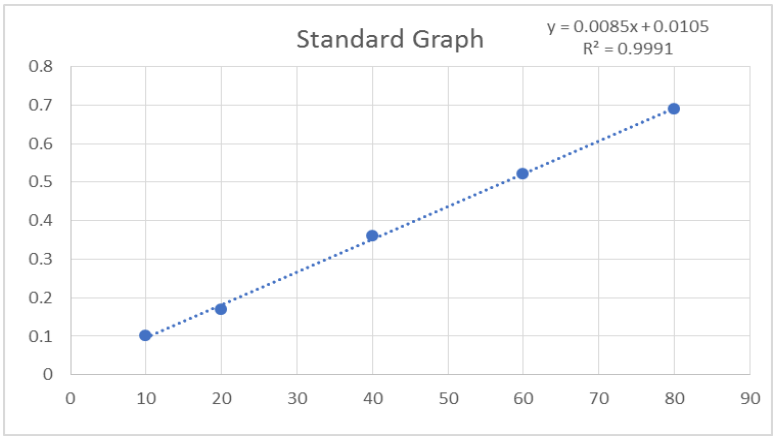

Fig 1: Standard graph of Salicylic acid crystals in water.

The equation of the graph was found to
y = 0.0085x + 0.0105,
with an R^2 square value of 0.9991.
Hence, the graph was found to be linear between 10 -80 µg/ml.

Dissolution studies of Salicylic acid Capsules and Compacts

Dissolution studies of salicylic acid capsules were performed using USP Type I and Type II apparatus and the drug release is shown in Table 2.

Table 2: Cumulative Drug release percentage of Salicylic Acid Capsule.

S.no	Time (min)	Drug Release (%) ± Mean in Paddle method	Drug Release(%) ± Mean in Basket method
1	15	62.86 ± 1.14	49.58 ± 1.42
2	30	77.50 ± 0.10	71.89 ± 2.11
3	45	80.78 ± 2.22	77.80 ± 1.20
4	60	69.80 ± 1.20	75.47 ± 1.53
5	75	84.47 ± 1.53	81.39 ± 1.61

Dissolution studies of salicylic acid compacts were performed using USP Type I and Type II apparatus and the drug release is shown in Table 3.

Table 3: Cumulative Drug release percentage in Salicylic acid Compacts.

S.no	Time (min)	Drug Release (%) ± Mean in Paddle method	Drug Release(%) ± Mean in Basket method
1	15	4.70 ± 0.30	5.43 ± 0.57
2	30	9.56 ± 0.44	10.89 ± 0.11
3	45	13.90 ± 0.10	15.48 ± 0.52
4	60	17.32 ± 1.68	19.19 ± 1.81
5	75	19.32 ± 1.68	23.37 ± 1.63

f1 & f2 Factors Calculation

Dissolution of salicylic acid capsules and compacts were performed using USP Type I and Type II apparatus.
Dissolution profiles of Type I & Type II apparatus were compared using difference factor f1 and similarity factor f2.

f1 for capsules was found to be 5.13 and f2 was 56.35.
f1 for compacts was found to be 12.85 and f2 was 80.71.

CONCLUSION

Salicylic acid compacts and capsules were prepared. Dissolution studies of their dosage forms were carried out using USP type I and type II apparatus. Comparison of dissolution profiles was done using f1 & f2 factors.

f1 & f2 value for the dissolution studies of salicylic acid compact and capsules using USP type I and type II apparatus followed the acceptance criteria. A notable difference in dissolution studies of salicylic acid was not observed. Hence, the two apparatus maybe interchangeable.

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