# FORMULATION AND EVALUATION OF AMPICILLIN TRIHYDRATE AND ACRYLIC RESINS CO-PRECIPITATE INTO A SOLID DOSAGE FORM

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## Abstract

The aim of this study is to formulate and evaluate the ampicillin trihydrate and acrylic resins co-precipitate as a sustained release solid dosage form. Three ampicillin tablet formulations designated T-I, T-II and T-III containing pure drug, drug/Eudragit$^{(R)}$ (1:1) and drug/Eudragit$^{(R)}$ (2:1) coprecipitates respectively were prepared in order to produce tablets with satisfactory quality suitable for comparative studies. Evaluation of compressed tablets was carried out and the results compared with standards given in the official books. Uniformity of content and dissolution rate studies were the parameters evaluated. A product is considered satisfactory when the evaluation results of the product are in conformity with the standards given in the official books. The uniformity of content was within (- 3.9% to +0.4% for T-I),(-6.1% to +0% for T-11) and (-9% to +0.4% for T-111) formulations respectively. These results are within the official acceptable specifications of ±15% for nine (9) tablets, with none exceeding ±25%. About 87%, 35.5% and 52.0% of drug dissolution were attained after one hour from formulations T-I, T-II and T-III respectively. Formulations T-II therefore shows a significant retardation in the drug release rate. The mechanism of drug release from these formulations (T-II and T-III) is by erosion. It appears that drug release profiles from T-II and T-III are closer to first-order kinetics than zero-order kinetics; this is due to gradual decrease in the tablet surface area due to erosion. The results of this study have shown a considerable influence of Eudragit-RS(R) on the retardation of the release rate of ampicillin trihydrate in the designed tablet formulation in a given set of *in vitro* study.

**Keywords:** *Formulation, Evaluation, Ampicillin trihydrate, Eudragit-RS®.*

## Introduction

In formulation of tablets, beside the active ingredients, other substances generally referred to as excipients are often incorporated to aid the processing of tablets such as flowability, compressibility, elegancy, delivery or release of its active component so as to make it bioavailable (Nystrom and Kavehill, 1996; HPE, 1994; Bangudu, 1993; Hyanjo *et al*., 1988). Drug with short biological half-life require multiple dosing which are often accompanied by patient's poor compliance which may lead to therapeutic failure and drug resistance in the case of antibiotics (Porter, 1969). Sustained release dosage form may be useful and convenient for such patients (Ballard and Nelson, 1975). Sustained release products have received considerable attention long time ago (Lazarus and Cooper, 1961; Ritschel, 1970; Cooper and Rees, 1972; Theeuwes, 1975). The solid dispersion technique has been applied by Ghanem *et al* (1980a and 1980b) in sustained release formulations of tetracycline and

chloramphenicol. The drugs were dispersed in an acrylic resin which is a water insoluble inert carrier. Recently Emenike and his colleagues (2016a) reported the physico-chemical characteristics of ampicillin trihydrate and a carrier (Eudragit-RS$^{(R)}$) in the formulation of sustained dosage form. Both the drug and the carrier (Ampicillin trihydrate and Eudragit-RS$^{(R)}$ respectively) were found to be appropriate in the formulation of sustained dosage forms. Thin layer chromatography and infra-red studies of the dispersed systems showed that the drug dispersions with Eudragit-RS$^{(R)}$ were stable (Emenike *et al*., 2016b). The in-vitro dissolution rate studies of the dispersed drug indicated a slower dissolution rate as compared with the pure drug. Emenike *et al* (2016b) also reported the dissolution rate for the Ampicillin trihydrate and Eudragit-RS$^{(R)}$ was slower for 1:1 than for 2:1 drug/polymer dispersions. Therefore, there is a need to formulate and evaluate the ampicillin trihydrate and acrylic resins co-precipitate into a solid dosage form. This is the aim of the present study

## Materials and Methods

### Formulation of ampicillin trihydrate tablets

Three ampicillin tablets formulation designated T-I, T-II and T-III containing pure drug, drug/Eudragit$^{(R)}$ (1:1) and drug/Eudragit$^{(R)}$ (2:1) coprecipitates respectively were prepared. The compositions used are not any of those used in commercial production; rather they are such that would produce tablets with satisfactory quality suitable for comparative studies. No comparison with existing commercial ampicillin solid dosage forms was made. The details of the tablet formulations are given in table 1.

Table 1: Ampicillin trihydrate formulations: Quantities used for one tablet in gram

| Ingredients | Formulations | | |
|---|---|---|---|
| | T-1 | T-II• | T-III* |
| Ampicillin Trihydrate (g) | 0.100 | 0.200 | 0.150 |
| Dextrose (g) | 0.048 | 0.040 | 0.040 |
| Microcrystalline cellulose (g) | 0.250 | 0.158 | 0.208 |
| Stearic acid (g) | 0.002 | 0.002 | 0.002 |
| Weight per tablet (g) | 0.400 | 0.400 | 0.400 |

•1:1 drug/Eudragit coprecipitate, *2:1 drug/Eudragit coprecipitate

Most of the excipients used in the table above (Table 1) were selected based on their compatibility with ampicillin trihydrate as reported earlier by El- Shattawy (1982). To facilitate direct compression, microcrystalline cellulose was found to be of additional importance. All the formulation ingredients with the exception of microcrystalline cellulose which was used as received were passed through a 150 µm sieve.

Required quantities of the pure drug or coprecipitate where applicable, necessary for 100 tablets were properly blended in a laboratory cube mixer for 10 minutes, after which quantities of dextrose and stearic acid were properly added and mixed for another 10 minutes. The homogeneous blends of ingredients for T-I, T-II and T-III formulations were directly compressed at 6 kgwt using a single punch tabletting machine (KORCH-Berlin, Type-EKO Erweka Apparatebau FRC) fitted with 10 nm flat punches. Tablets weighing approximately 400 mg were made from each of the formulations. The tablets were stored in a desiccator containing anhydrous calcium chloride till further studies.

**Evaluation of ampicillin trihydrate tablet formulations**

Evaluation of compressed tablets is usually carried out and the results compared with standards given in the official books. The results of this evaluation are used to assess the total quality of a given product. A product is considered satisfactory when the evaluation results of the product are in conformity with the standards given in the official books (BP, 1980; BP, 2002).

**Uniformity of content**

Ten tablets were picked at random from each batch and individually assayed. Each tablet was powdered and portions enough to contain about 10 mg of pure drug carefully weighed out and dissolved in 100 ml of buffer A. The assay of the drug in the sample was based on the spectrophotometric method according to the procedure described by Smith *et al.* (1967). According to BP (2002) 10 tablets should be assayed and at least 9 should contain ±15% of the declared amount and none may exceed ± 25%.

Method of Calculations; A = (Absorbance – Intercept)/Slope x D x Wt. of tablet (mg)/Sample wt (mg). Where D is the dilution factor and A is the active ingredient for tablet. The theoretical active ingredient content of each tablet is 100 mg.

**Dissolution rate studies**

Tablet dissolution rate studies were carried out using the BP (2002) method with slight modification. One tablet sample was placed in the basket held at 3 cm from the bottom of a 500 ml beaker containing 400 ml of
distilled water equilibrated at 37±0.5$^{o}$C. The basket rotation speed was 100 rate per minutes (rpm). After the following time intervals, (5,15,30,60,90,150,210,270,390,), 5 ml samples were withdrawn from a fixed position in the dissolution medium and replaced with equivalent amount of distilled water maintained at the same temperature. The sample solutions were filtered using millipore filter HA 0.45 µm (millipore corp. USA) and 1 ml of the filtrate was diluted to 20 ml using the buffer-A solution. Assay of the drug in the diluted samples was based on the spectrophotometric method described earlier. The percentage cumulative drug concentrations were calculated base on the mean absorbances of three runs for each batch.

## Results and Discussions

Three different batches of 400 mg ampicillin trihydrate T-I, T–II and T-III were formulated as shown in Table 1.

**Table 2: Content uniformity test for Ampicillin trihydrate tablet (mg)**

| *Tablets* | *Formulations* | | |
|---|---|---|---|
| | ***T-I*** | ***T-II*** | ***T-III*** |
| 1 | 97.9 | 96.0 | 91.0 |
| 2 | 96.7 | 93.9 | 92.0 |
| 3 | 99.7 | 94.7 | 104.3 |
| 4 | 100.4 | 94.3 | 103.7 |
| 5 | 99.1 | 93.9 | 91.6 |
| 6 | 96.9 | 93.7 | 90.9 |
| 7 | 96.1 | 94.5 | 110.8 |
| 8 | 99.2 | 96.2 | 104.7 |
| 9 | 97.2 | 93.9 | 108.7 |
| 10 | 96.2 | 96.0 | 110.0 |

The tablets from the three batches were evaluated and the result obtained conformed to the official specification of similar tablets. The uniformly of content values as shown in table 2 conforms with the BP (2002) specifications of ±15% declared content of at least nine (9) tablets and none exceeding ±25% (i.e between ±15% to ±25%). T-I had 3.9% to +0.4%, T-II and T-III had -6.4% to 0% and -9% to + 10% respectively. The result shows that active ingredient (ampicillin tryihydrate) content of the tablets in all the formulations were within the acceptable deviation from the 100 mg theoretically assumed weight. The tablets in respect of uniformity of content were considered satisfactory since the values were between – 2.19 to +10% which is within the ±15% to ±25% official standards.

**Table 3: Dissolution rate of Ampicillin trihydrate in water at 37 ± 0.5°C**

| | % Dissolved | | |
|---|---|---|---|
| ***Time (min)*** | ***Formulations*** | | |
| | ***T-I*** | ***T-II*** | ***T-III*** |
| 5 | 21.0 | 6.0 | 13.0 |
| 15 | 56.5 | 16.2 | 24.0 |
| 30 | 74.0 | 25.0 | 43.9 |
| 60 | 87.1 | 35.5 | 52.0 |
| 90 | 93.9 | 40.3 | 61.5 |
| 150 | 99.0 | 55.3 | 77.0 |
| 210 | 100.0 | 65.0 | 90.5 |
| 270 | - | 72.8 | 93.0 |
| 390 | - | 79.0 | 95.1 |

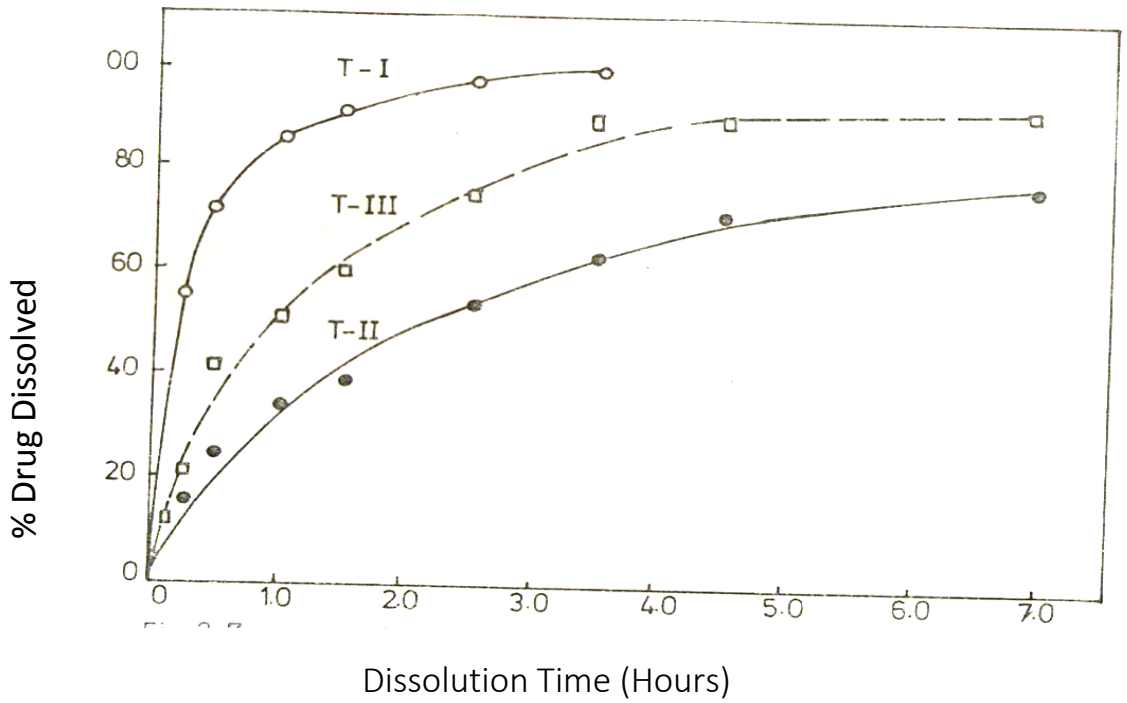


Figure 1: dissolution rate profiles of ampicillin trihydrate tablets containing various concentrations of the drug (T-I pure drug = ○; T-II drug/EudragitRS 1:1 = ●; T-III drug/EudragitRS 2:1 = □)

The dissolution rate profile of ampicllin tryhydrate tablets containing various concentration of the drug is shown in table 3 and figure 1. It can be seen that about 87%, 35.5% and 52% of drug dissolution were attained after one hour from formulations T-I, T-II and T-III

respectively. Formulations T-II therefore showed a significant retardation in the drug release rate, which is in agreement with Ghanem *et al* (1980a and 1980b). Considering the drug release rate from formulations T-II and T-III at one hour time interval, the ratio or concentration of Eudragit (R)-RS used in the formulation played a significant role in the retardation of drug release. After 210 minutes, 100% drug dissolution was attained for formulation T-I, while 65% for T-II and 90.5% for T-III respectively. At 390 minutes, 79% and 95.1% drug dissolution were attained for T-II and T-III formulations respectively. Formulation T-II, which has a higher amount of the acrylic resin (1:1, drug-resin ratio), maintained the slowest dissolution rate throughout the studies. This shows that the higher the resin ratio, the slower the retardant effect. The result of the present study is in complete agreement with the report of Emenike and his colleagues (2016b) in which both ampicillin and the polymer Eudragit-RS$^{R}$ was found to be stable in tablet formulation. The mechanism of drug release from these formulations (T-II and T-III) is by erosion. This erosion rate decrease, in the polymer (Eudragit-RS$^{R}$) ratio, thus a slower release rate of the drug was obtained for formulation T-II than for formulation T-III. It appears that drug release profiles from T-II and T-III are closer to first-order kinetics than zero-order kinetics this is due to gradual decrease in the tablet surface area due to erosion. As a result of better *in-vitro* retardation effect, formulation T-II was suggested for further studies in the human subjects.

## Conclusion

The results of this study have shown a considerable influence of Eudragit-RS on the retardation of the release rate of ampicillin trihydrate in the designed tablet formulation. Formulation T-II had better in-vitro retardation activities and thus suggested for further in-vivo studies.

## Acknowledgement

The authors are sincerely thankful to laboratory staff of the Department of Pharmaceutics and Pharmaceutical Microbiology, Faculty of Pharmaceutical Sciences, Ahmadu Bello University Zaria, Nigeria for their technical assistance and support.

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