Experimental modeling for quality evaluation and rational Utilization of Diclofenac Sodium and Amoxicillin Trihydrate

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Abstract

We gathered 46 distinct generic versions of AMOX, including 43 capsule varieties and 2 250-milligram tablet forms. From them, we gathered one capsule product from each of two batches, for a grand total of 46 items. At a similar vein, 32 DICLO items were purchased without a prescription from a wholesaler or merchant in a market in a Northern Indian city or town. Amoxicillin is a low-toxicity, broad-spectrum penicillin that is used to treat a wide variety of infections in a wide variety of animal species. Amoxicillin is widely used in the poultry industry for the diagnosis, treatment, and prevention of a variety of illnesses. There are limitations to its therapeutic use in these species due to its short half-life and limited bioavailability.

Keywords: *Diclofenac Sodium, Amoxicillin Trihydrate, Rational, Animal treated.*

1. INTRODUCTION

There has been a dramatic drop in South Asian vulture populations (by 95% or more since 1993), and scientists believe that veterinary usage of diclofenac sodium, an NSAID, may be to blame. Because these birds scavenged on a corpse of an animal that had been given diclofenac sodium, they were exposed to the drug. The scavengers had perished of renal failure caused by visceral gout owing to diclofenac's relay toxicity. This review article provides a concise summary of the substantial ecological damage caused by the pharmaceutical substance diclofenac sodium and the subsequent discovery of meloxicam as a safe and eco-friendly alternative in veterinary practice. Amoxicillin is a low-toxicity, broad-spectrum penicillin that is used to treat a wide variety of infections in a wide variety of animal species (Palmer et al., 1976; Keefe, 1977). They provide it in two forms: a sodium salt, which is highly soluble in water, and a trihydrate salt, which is less soluble. Parenteral administration of amoxicillin trihydrate is a viable option for treating bacterial infections in animals. It produces a suspension that remains in the body for a longer period of time and is more stable than sodium amoxicillin.

2. LITERATURE REVIEW

Magdalena Janczura et.al (2022) The multilayer tablet press, polymers for pharmaceutical uses, the hot-melt extrusion method, and 3D printing in the pharmaceutical business are all directly tied to the creation of novel forms of combination medications. Nonetheless, significant physicochemical and pharmacodynamic interactions might arise from the concurrent use of different medications in the same dose form. Overcoming the incompatibility of active ingredients or obtaining diverse drug release characteristics in the same dosage form have spurred the development of novel fixed-dose combinations (FDCs). While discussing the characteristics of the key ingredients in the FDC formulation and presenting technological problems and challenges related to the development of combination drugs, this review discusses the application of various innovation formulation technologies of FDC drugs, such as the bilayer system, multilayer tablet, active film coating, hot-melt extrusion, and 3D printing. In addition, the article provides a brief overview of the many dosage forms that have been produced with the use of these technologies during the previous three decades.

Ikbal Taleb et.al (2021) For public and commercial organizations to make informed analytics choices, Big Data research is crucial. Data collection, processing, and analysis in order to derive insights and make choices based on the data are all aspects of Big Data. Consequences of a drop in Data Quality might be surprising. When this happens, people lose faith in the information and its reliability. The danger of quality deterioration and the need for effective processes to assess data worthiness are exacerbated in the Big Data setting by properties of the data itself, such as volume, diverse data sources, and rapid data production. However, because of the extensive

computer resources needed, maintaining Big Data Quality (BDQ) is a very time-consuming and expensive endeavor. Prior to making a processing choice, quality must be profiled and verified in order to maintain it throughout the Big Data lifecycle. As a means of better managing data and facilitating pre-processing operations, we recommend a BDQ management framework. Big Data Quality Profle is a novel idea used in the suggested framework. The idea includes a summary of the quality's structure, criteria, qualities, dimensions, ratings, and regulations. Before and after an intermediate pre-processing phase, the system uses Big Data profiling and sampling components to launch a quicker and more efficient data quality assessment. Quality profiling begins with the framework's exploratory profiling component, which employs a defined set of quality metrics to rate key aspects of data quality. By carrying out a number of pre-processing operations and associated services, it produces quality norms. Quality scores for the chosen quality characteristics are the end result of applying these rules, which are primarily directed at the Data Quality Profile. Some continuing work on framework assessment and deployment to assist quality evaluation choices has also been presented, along with the installation and dataflow management of frameworks across many quality management processes. to wrap up the paper.

Rudy Sofyan ET.AL (2019) Every effort made in the translation process should be directed toward achieving the highest possible quality. However, there are a variety of approaches to determining whether or not a translation is adequate, collectively referred to as translation quality evaluation (TQA). Many TQA models openly acknowledge the problem of relativity and subjectivity. The purpose of this research is to provide a comprehensive TQA for evaluating English to Bahasa Indonesia translation. For this investigation, researchers opted for a developmental strategy. Both first-hand observations and previously collected data were used. The study report was secondary data, whereas the main data came from the interviews and FGD. An interactive model was used to examine the data. According to the results of this study, I a holistic approach is the best foundation for TQA, (ii) a holistic TQA model should give distinct quality criteria, and (iii) the TQA model created here evaluates both translation and linguistic competence. The results of this research indicate that a comprehensive TQA should account for both linguistic and translational criteria for a high-quality final product.

E. Güncüm et.al (2018) In the poultry industry, amoxicillin is used for both the treatment and prevention of a variety of infections. However, its therapeutic use in these species is limited by its short half-life and poor absorption. The oral bioavailability and gastrointestinal absorption of medications may be enhanced by entrapping them in polymeric nanoparticles (nps). The purpose of this research was to find a way to make amoxicillin more useful in chicken farming. Preparation and characterisation of nps loaded with amoxicillin and made from a sodium alginate-polyvinyl alcohol (NaAlg-PVA) mix were carried out. Commercial male broilers were utilized to compare the pharmacokinetics of amoxicillin in both its free and nanoparticle forms. We split up twenty-one broilers into three groups. The standard dose for all groups was 10 mg/kg. We took plasma samples from patients and analyzed them using high-performance liquid chromatography. Based on the findings, the nps had a particle size of 513.96 19.46 nm, a zeta potential of 45.36 1.35 mV, an encapsulation efficiency of 43.66 3.30, and a loading capacity of 12.06 0.83%. An initial 18% was released in a burst within 2 hours, followed by a steady release over 22 hours, as seen in in vitro drug release. The pharmacokinetic data shown that compared to free amoxicillin, amoxicillin nps had significantly greater bioavailability and a longer plasma half-life (p .01). These findings support the use of an oral formulation of amoxicillin nanoparticles in broilers.

Krzysztof Ejsmont et.al (2017) This article demonstrates an approach to evaluating intelligent manufacturing systems that may be put to use in many contexts. The evaluation takes into account the economy, society, and environment as a whole, assuming a paradigm in which they are all in harmony with one another. The suggested approach draws inspiration from both Prof. Marciniak's integrated technique and the notion of controlling. This article presents a hybrid of these two methods, illuminating the comprehensive evaluation strategy developed specifically for intelligent technology. Because of this, the new solution incorporates features that were absent from the traditional approach. So yet, there is no description of the suggested evaluation in the scholarly canon.

3. METHODOLOGY

Bacterial strain. In order to assess the MIC and MBC100, an in-vitro test was performed using a penicillin-susceptible Staphylococcus aureus strain (ATCC 25923) cultured in Mueller-Hinton broth (Merck, Darmstadt, Germany) and Salt Mannitol agar (Merck, Darmstadt, Germany). The microbiological test of amoxicillin concentrations and the regression line assay both employed the same strain.

Drugs. Sigma Chemical Co. supplied the amoxicillin trihydrate used in this study (St Louis, MO, U.S.A.). Both the betamethasone and the diclofenac sodium were purchased from pharmaceutical companies. (Celestone injectable® - Schering-Plough S/A and Voltaren injectable® - Novartis Biociências, respectively.) The animals used as controls were given a 0.9% sodium chloride solution (physiological saline).

Regression line: Using rat serum that had been washed clean of any drugs, amoxicillin suspensions of concentrations 0.03, 0.05, 0.07, 0.10, 0.30, 0.50, 0.70, 1.0, 3.0, 5.0, 7.0, and 10 g/mL were prepared and 10 L was spotted onto dry paper-filter discs (6.25 mm). Mueller Hinton agar was infected with 108 cfu/mL of S. aureus, and three discs of each concentration were then put on the agar. After incubating at 37 degrees Celsius for 18 hours, the resultant inhibitory zones were measured in millimeters. The regression line was calculated using these intervals and the amoxicillin concentrations (Excel XP® - Microsoft Corporation).

Generic products collection

Forty-six AMOX generic goods were gathered, including 43 capsule varieties and 2 tablets with a 250 mg dosage. Two batches of the capsule product were gathered, for a grand total of 46 items. Additionally, 32 DICLO products were bought without a prescription from wholesalers and retailers in urban and semi-urban regions of Northern India.

Amoxicillin standard and sample preparation

Procedures for establishing an Amoxicillin Reference Standard and for Preparing Representative Samples Each lot was manufactured in accordance with the amoxicillin capsule monograph published in the 2010 edition of the Indian Pharmacopoeia (IP). In each sample, we compared ten units of each product (capsules). The amount of amoxicillin in the test sample was calculated by comparing the label claim per capsule to the average area of five injections of AMOX RS. Standard quality requires an assay result that is between 89.5% and 110.6% of the label claim per IP, and between 84.5 and 100% of the claim per CDSCO.

Ten tablets of each DICLO product were dissolved in 100 mL of amber-colored volumetric flask to achieve a DICLO concentration of about 0.20 mg per mL. There was a hard limit of 2% on the %RSD between the two preparations used in the test, allowing for more accurate calculations of the final diclofenac concentration. Each product's test value must range from 89.3 percent to 110.8 percent in order to meet the pharmacopeia definition. Contrarily, NSQs are defined by CDSCO as products with test results that are more than 5% below the pharmacopoeia specification of 84.3%.

4. DATA ANALYSIS

Amoxicillin's MIC and MBC100 against S. aureus ATCC 25923 were 0.2 g/mL and 1.5 g/mL, respectively.

The detection limits of the regression curve were 0.03 g/mL (12 mm of inhibition zone diameter) and 10 g/mL, respectively (31 mm of inhibition zone diameter). R = 0.9851 indicated a linear relationship between the diameter of the inhibition zone (DIZ, in mm) and the concentration of amoxicillin (CA, in g/mL) using the formula DIZ = (3.23 x Ln (CA)) + 24.16. Considering the average tissue weights of all the animals, this relation was utilized to determine tissue and serum concentrations.

For the granulomatous tissue samples, the mean standard error of the mean (mg) wet weights were as follows: 30.2 (1.98), 42.8 (3.26), 40.2 (1.98), 31.2 (2.58), 46.5 (3.8), and 41.1 (2.22). Wet weight readings showed no statistically significant differences between groups ($p>0.05$).

There was a clearly defined fibrous capsule around the sponge in all samples taken at the 7 day and 90-minute mark. Extensive evidence supported the presence of fibroblasts, mesenchymal cells, and new capillary development. None of the granulomatous tissues showed signs of infectious exudate.

The amounts of amoxicillin in the serum and tissues of groups 1, 4, and 5 are shown in Figure 1. When looking at both blood and tissue samples, groups 2, 3, and 6 did not have an inhibitory zone during the microbiological experiment. These prohibition zones were seen only in the amoxicillin-treated groups. The concentration of amoxicillin in serum and tissue was not altered by betamethasone ($p>0.05$). However, diclofenac sodium caused a decrease in amoxicillin concentrations in both serum and tissue (p0.05).

The S. aureus ATCC 25923 strain was found to be susceptible to amoxicillin based on its MIC and MBC100 values14. Since it has been noted in

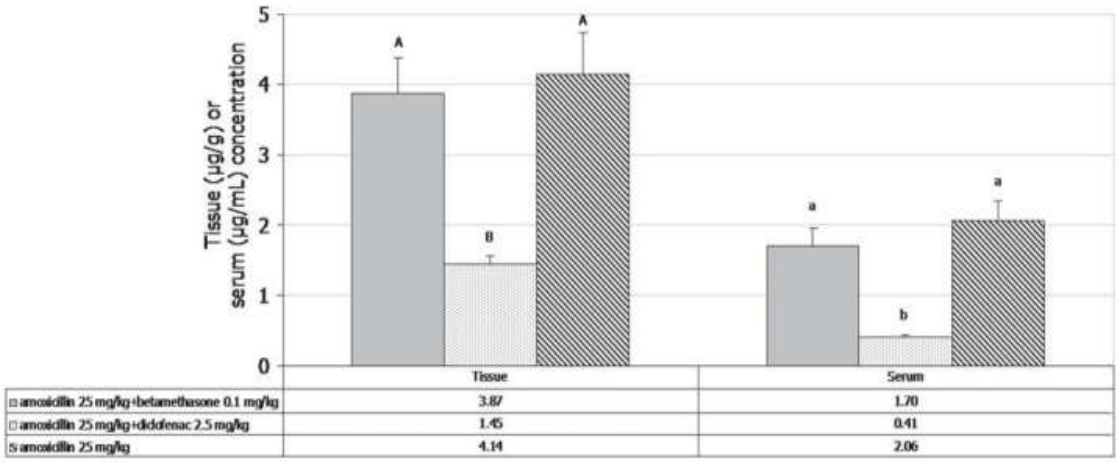

Figure 1- Amoxicillin serum and tissue concentrations (mean ± s.e.m.) considering groups 1, 4 and 5. Groups 2, 3 and 6 did not show any inhibition zone considering both serum and tissue samples. Different letters mean statistically significant differences ($p<0.05$) among groups, considering serum and tissue concentrations separately

Microbiological methods have been shown to be reliable for measuring amoxicillin concentrations in prior research. This technique has been extensively used to determine amoxicillin concentration, and its accuracy is comparable to that of HPLC assay17.

Based on the findings of the 7-day time frame utilized here to allow granulomatous tissue to mature is sufficient. This group of researchers found that the pharmacokinetics of amoxicillin were not affected by the length of time (7, 14, 21, or 28 days) that rats were allowed to develop granulomatous tissues.

Betamethasone and diclofenac sodium have been shown to have strong anti-inflammatory action in both humans2 and rats24. While in previous models anti-inflammatory drugs with or without amoxicillin were able to lower tissue wet weights, in the current model they were not. Chronic inflammatory granulomatous tissue may not have been the best model to investigate anti-inflammatory effects. Also, the inflammatory cells, as measured by the wet weight of the granulomatous tissues, may not be reduced by a single dosage.

The match plot at 230 nm revealed the presence of the AMOX RS peak, demonstrating the system's capability for regular analysis. The peak purity was evaluated with a stricter purity threshold than the purity angle. We confirmed the presence of amoxicillin in the capsules and determined the percentage of amoxicillin based on the label's claim. 13 goods out of a total of 46 had percentages that did not match what was stated on the label. Products did not match the IP requirements, as seen in Fig. 2. Six goods did not meet the CDSCO threshold for safety. As a result, 13.04% of items were deemed inferior, while 28.26% of products did not conform to IP specifications.

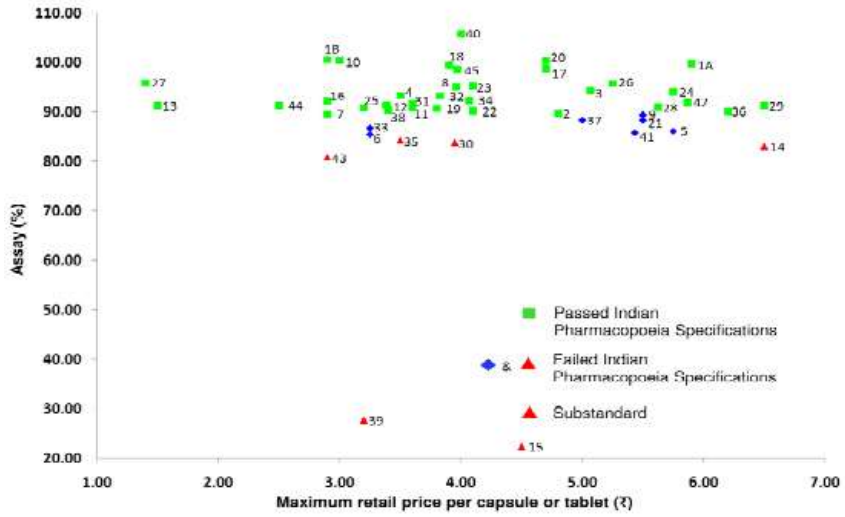

Fig. 2 Maximum retail price versus mean assay plot showing amoxicillin generic products (N=46) quality

The examined products' assays and prices did not vary significantly using Fisher's exact test (two-tailed p-value = 0.87). It's safe to say that many things now for sale are of low quality. Table 1 shows that there is no correlation between price and quality beyond the extremes.

Table 1 Price wise distribution of passed and failed AMOX products

Maximum retail price per capsule/tablet (₹)	No. of products failed	No. of products passed
1-2	-	2
>2-3	1	5
>3-4	6	11
>4-5	2	5
>5-6	4	6
>6-7	1	2

Diclofenac Sodium

The suggested approach was verified at the Q2 (R1) level according to the ICH recommendations. Of the 32 goods tested, 34.37 percent did not meet the pharmacopoeia specification, and 15.62 percent fell into the "Category B" quality range, as defined by the Central Drugs Standard Control Organisation (CDSCO) in New Delhi. Prices do not always indicate quality, as illustrated in Fig. 3, which shows that neither high nor cheap prices necessarily indicate either high or low standards. Fisher's exact test found that there was no statistically significant relationship between price and assay value, yielding a p-value of 0.43 on a two-tailed test. It shows that low-priced and high-priced items of inferior quality are both available on the market. Table 2 shows that there is no statistically significant relationship between high severity of the underlying condition and cheap cost alone.

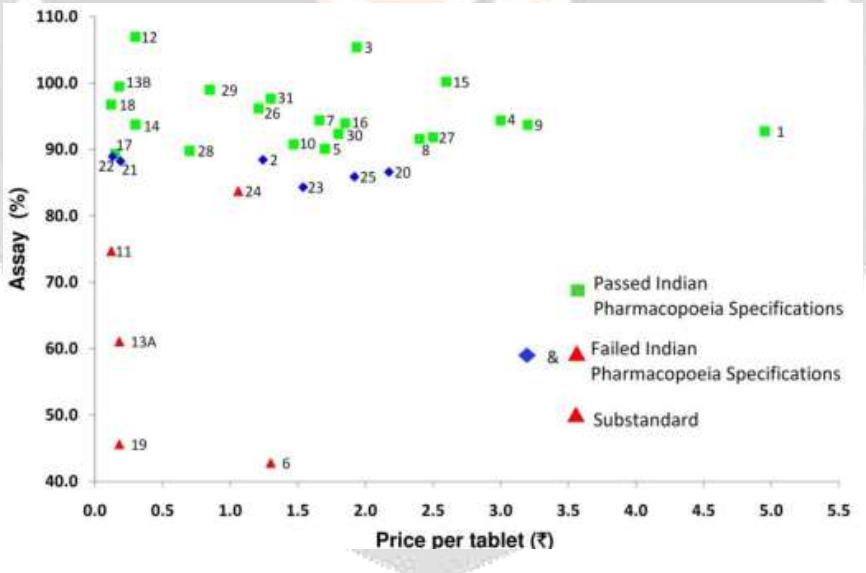

Fig. 3 Maximum retail price versus mean assay plot showing diclofenac generic products (N=32) quality

Table 2 Price wise distribution of passed and failed DICLO products

Maximum retail price per tablet (₹)	No. of products failed	No. of products passed
0.1-0.5	5	5
>0.5-1	-	2
>1-2	5	8
>2-3	1	3
>3-4	-	2
>4-5	-	1

5. CONCLUSION

To better track down issues with goods' quality and effectiveness as they make their way across the market, the methodology will allow authorities to create and adopt a dynamic and active strategy. Since no recent research has focused on the quality of medications on the market, it is unclear how widespread the problem of low-quality or substandard pharmaceuticals really is. Poor quality generic versions of amoxicillin were found to be 28.26% (N=46) and diclofenac 34.37% (N=32) prevalent in the Indian market. The regulatory authorities are concerned about the possible consequences of such low dosage drugs. Poor manufacturing and quality control methods, or purposefully faked pharmaceuticals, have resulted in an urgent need to address the availability of inferior drugs on the market. India is lagging behind other countries in addressing the problem of counterfeit and low-quality pharmaceuticals, which has received increased attention elsewhere. Accordingly, there is an urgent need for further study or regular analytical evidences to explain the size of the problem of fake and low quality pharmaceuticals throughout India. The results showed that serum and tissue amoxicillin concentrations were unaffected by betamethasone, but were considerably decreased by diclofenac sodium.

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