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Comparative evaluation of chemical equivalence of some commercially available brands of Gatifloxacin tablet

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Abstract

This study was undertaken with the objective of evaluating of six brands of Gatifloxacin tablets and the chemical equivalency with the use of an analytical method, which will be easy to use, accurate, reproducible, simple, and inexpensive. The chemical equivalence of six brands of Gatifloxacin tablets were assessed through the non-aqueous titration procedure with the use of crystal violet solution indicator. The non-aqueous titrimetric procedure showed that the excipients did not affect the procedure; with three brands having values within the range specified. While the remaining three brands gave lower values. The non-aqueous titrimetric procedure used in this study is simple, inexpensive, and easy to use and could be used in routine monitoring of the quality of Gatifloxacin tablets, especially in the absence of high technology equipments that are not easily available in most developing countries.

Key-Words: Gatifloxacin tablets, non-aqueous titration, chemical equivalence

Introduction

Gatifloxacin sold under the brand names Gatiflo, Tequin and Zymar, is an antibiotic of the fourth-generation fluoroquinolone family,that like other members of that family, inhibits the bacterial enzymesDNA gyrase and topoisomerase IV. Bristol-Myers Squibb introduced Gatifloxacin in 1999 under theproprietary name Tequin for the treatment of respiratory tract infections, having licensed the medication from Kyorin Pharmaceutical Company of Japan. Allergan produces an eye-drop formulation calledZymar. In many countries, gatifloxacin is also available as tablets and in various aqueous solutions forintravenous therapy. Gatifloxacin is currently available only in the US and Canada as an ophthalmic solution. In China it is sold in tablet as well as in eye drop formulations. Gatifloxacin was banned in India on the 18th of March along with Tegaserod. A statement from the health ministry said: 'The use of the following drugs is likely to involve certain risks to human beings, whereas safer alternatives to the said drugs are available.

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The move comes after international studies revealed that Gatifloxacin posed 17 times higher risk of developing serious hyperglycemia (high blood sugar) than other antibiotics in elderly patientsThe introduction of generic drug product from multiple sources into the health care delivery system of many developing countries was aimed at improving the overall healthcare deliverysystems in such countries. However, this has been accompanied by a variety of problems of which the most critical is the widespread distribution of fake and substandard drug products. The need to select one product from among several generic drug products of the same active ingredients during the course of therapy is a cause of concern to a healthcare practitioner. The first stage in ascertaining the therapeutic equivalence of any drug product involves ascertaining the chemical and biopharmaceutical equivalency of such drug product[1-4]. The objective of this study was to evaluate the chemical equivalence of six brands nimusilide tablets of an analytical method, which will be easy to use, simple, and in expensive with results, which compare favourably with established official methods.

Material and methods

Gatifloxacin pure powder was a gift from Windlass Pharmaceutical Industry, Dehradun while the various brands of the tablets were obtained from retail Pharmacies Dehradun, Reagents used include *g*lacial

acetic acid, perchloric acid, acetic anhydride, potassium hydrogen phthalate, hydrochloric acid, crystal violet solution. Six different brands of Gatifloxacin tablets and the innovator brand with labeled contents of 100mg each. [5-8]

The percent of Gatifloxacin was determined by applying the following equations:-

$$M_1V_1=M_2V_2$$

$$M_2= \frac{M_1V_1}{V_2}$$

Where, M_2=Molarity of Gatifloxacin in sample solution, M_1= Molarity of perchloric acid, V_1=Volume of perchloric acid , V_2=Volume of sample solution

Strength of Gatifloxacin (gm/ml)
= Mol. Wt of Ciprofloxacin HCL X M2
1000
Percentage of Gatifloxacin
= wt of Gatifloxacin in sample solution X 100
500

Chemical content determination

Gatifloxacin pure powder*:* - 0.1g, 0.2g and 0.3g were dissolved in glacial acetic (15ml) acid, followed by the addition of freshly prepared mercuric (II) acetate solution (0.5ml, 1.0ml and 1.5ml respectively) and acetic anhydride (2ml,4ml and 5ml respectively). The solutions were titrated against 0.1M acetous perchloric acidusing 0.5%w/v crystal violet solution as indicatoruntil a bluish – green end point.Blank titrations were carried out using 15ml glacial acetic acid. Titre values were adjusted by deducting the blank determination from the assay. This was carried out in triplicate Gatifloxacin *tablets* (Innovator brand):- Amounts of the crushed tablet material equivalent to 0.1g, 0.2g, 0.3g of pure Gatifloxacin in the tablet dosage form of the innovator brand were weighed.These were dissolved in 15ml glacial acetic acid, followed by the addition of freshly prepared mercuric (II) acetate solution (0.5ml, 1.0ml and 1.5ml respectively) and acetic anhydride (2ml,4ml and 5ml respectively). The solution was titrated against 0.1M acetous perchloric acidusing 0.5%w/v crystal violet solution as indicator until a bluish – green end point. Blank titrations were carried out using 15ml glacial acetic acid. Titre values were adjusted by deducting the blank determination from the assay. The procedure was carried out in triplicate. The procedure was then applied to ten other brands of Gatifloxacin tablets sourced from various pharmacy outlets.

Results and Conclusion

The result of the non-aqueous titration of Gatifloxacin pure powder at 0.1g, 0.2g and
0.3g and the equivalent weights of the powdered tablets of the innovator brand is presented in Table1. The values obtained with the different concentrations showed that the excipients did not affect the procedure.

The chemical content determination procedure used in this study involves the modification of the non-aqueous titration specified in B.P for Gatifloxacin HCl pure powder. The modification involves the addition of acetic anhydride and mercuric (II) acetate solution, using 5%w/v crystal violet solution as indicator. The application of the non-aqueous titrimetric procedure was based on the following equation;

$C_{19}H_{22}FN_3O_4 + Hg(OAc)_2 + HClO_4$---------- $2C_{19}H_{22}FN_3O_4.H+ + HgCl2 + 2CH_3COOH + 2ClO_4$

The Gatifloxacin pure powder at 0.1, 0.2 &0.3g gave 99.12 ± 1.48,100.17 ±1.54 &
100.37±1.03%w/w respectively which is in line with the USP 1990 specification of 90 –
110%w/w. Similarly, equivalent weights of the powdered Gatifloxacin tablets (innovator
brand) gave 99.97 ± 2.78, 98.01 ± 1.89 & 100.27 ± 2.05w/w respectively. The procedure was repeatable with consistent results and very good interday and intraday precision. The excipients of the tablets did not interfere with the assay procedure and result as the colour end point was clear and stable.

The non- aqueous titrimetric procedure for the assay of Gatifloxacin used in this study is simple, inexpensive, reproducible and easy to use and could be used in routine monitosring of the quality of Gatifloxacin pure powder and tablets, especially in the absence of high technology equipment that are not easily available in most developing countries.

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Table 1: Gatifloxacin content of pure and innovator brand of Gatifloxacin tablet as determined by non-aqueous titration using acetous HClO4 as titrant and crystal violet as indicator

Weight of sample (pure powder / equiv wts of tab.) (g)	Pure Gatifloxacin powder	Powdered Gatifloxacin tab. (Innovator brand)
0.1	99.82 ± 1.48	99.97 ± 2.78
0.2	100.60 ±1.54	100.01 ± 1.89
0.3	100.58 ± 1.03	100.27 ± 2.05

Table 2: Gatifloxacin content of six brands of Gatifloxacin tablets as determined by non-aqueous titration using acetous HClO4 as titrant and crystal violet as indicator

S/No.	Product Name and Brand	% Purity
1.	GATTY-400 by Dr. Reddy's	100.60
2.	GATIMAC-400 by Macleod's	100.58
3.	GATIKIND-400 by Mankind	99.97
4.	GATQUIN-400 by Cipla(solan)	100.60
5.	AUSGAT-400 by Austin Pharma	100.01
6.	Q-CAT by Cipla(Mumbai)	100.27