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Research Article

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Evaluation Invitro of the Suspending Properties of *Anogeissus Leiocarpus* Gum in Cefixime Trihydrate Oral Suspension

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ABSTRACT

This study was designed to formulate and develop the cefixime trihydrate 100 mg oral suspension using Anogeissus Leiocarpus gum as suspending agent, and its in-vitro quality evaluation. Dry direct mixing method was adopted for preparation of suspensions using different excipients namely; sodium benzoate, strawberry flavour, sucrose, areosil and Anogeissus Leiocarpus gum. The suspensions were evaluated for pH, density, sedimentation, rheological assessment; also, suspensions were subjected to assay in vitro studies. The formula was satisfactory per cefixime trihydrate 100 mg oral suspension properties and complied with the USP pharmacopoeia standard requirements when compared with marketed products.

Keywords: *Anogeissus leiocarpus* gum; Viscosity; Suspension; Cefixime trihydrate; Marketed products

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INTRODUCTION

A pharmaceutical suspension defined as an intimate mixture of dry, finely divided drug with excipients, which, upon the addition of suitable vehicle, yields a suspension [1]. *Anogeissus Leiocarpus* gum was chosen as the suspending agent for the suspension formulations; the proportions of the various chemicals in gums vary widely. Still, it remains an important ingredient in soft drink syrups, "hard" gummy candies such as gum drops, marshmallows, M&M's chocolate candies—and edible glitter, a popular modern cake-decorating staple. For artists, it is the traditional binder in watercolor paint, in photography, and it is used as a binder in pyrotechnic compositions. Pharmaceutical drugs and cosmetics also use gums as a binder, emulsifying agent, and a suspending or viscosity builders.[2]

The chemical formula of Cefixime trihydrate is C16H15N5O7S2, 3H2O and molecular weight 507.50 as the trihydrate [3, 4].

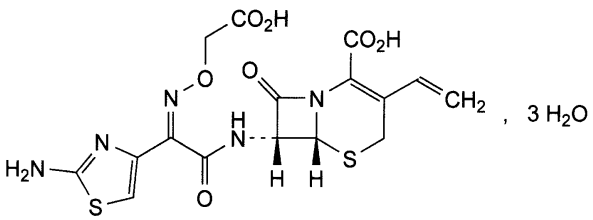


Figure 1: The structure of Cefixime trihydrate

The chemical structure of cefixime consists of the cephem nucleus, a β-lactam ring fused to a 6-membered dihydrothiazine ring. The cephem nucleus incorporates two important groups: the vinyl group at the 3-position, other groups are the aminothiazole ring and the acetic acid oxy-imine group on the side chain at the 7-position [5].
The chemical name of cefixime trihydrate [6] is 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-[[(2-amino-4-thiazolyl) [(caroxymethoxy) imino] acetyl]amino]-3-ethenyl-8-oxo trihydrate.[7, 8].
Cefixime is an orally active semi synthetic third generation cephalosporin antibiotic [9,10]. Cefixime has potent antibacterial activity against a wide range of bacteria, highly stable towards β-lactamases and and has a long duration of action [11]. Memon et al. reported that cefixime is a safe, effective, and cheaper oral option for the treatment of multidrug-resistance [12].

EXPERIMENTAL SECTION

Materials

Cefixime Trihydrate BP powder (Covalent Laboratories Private Limited. India).
The excipients sodium benzoate BP (Tiajin Dongda Chemical Group Co., China), strawberry flavor IH (LUNA CO. manufacturer. Egypt), sucrose USP (Kenana sugar Co., Sudan), areosil 200 USP (Transmare antwerpen N.V. India) and Anogeissus Leiocarpus gum (Gum belt, Sudan).

Methods

Preparation of cefixime oral suspension:
Table 1 shows the ingredients used to prepares cefixime trihydrate oral suspension, the suspension was prepared by direct dry mixing method. The calculated amount of active ingredient was weighed and manually sieved through 18 mesh screen (1 mm) and kept in a polyethylene bag. All other excipients were sieved through 18 mesh and kept in polyethylene bag. Mixture was manually blended for 5 minutes. Then the blend was sieving through 18 mesh. Finally, the powder was transferred to 75 ml amber bottles tightly closed.

pH measurement:
The pH of cefixime trihydrate 100mg oral suspension powder in distilled water, was measured using calibrated pH-meter (Sartorius, Model: Professional meter PP-20), directly in a homogenate prepared with bottle containing 15% (w/v) also pH values were measured for marketed product.

Specific gravity:
Specific gravity of the cefixime trihydrate 100 mg oral suspension powder and marketed product in distilled was determined as the procedure of described at (PB, 2013) using standardized pycnometer.

Sedimentation volume:
Sedimentation volume of the suspensions and marketed product was determined by measuring the volume of the sediments in the suspension placed in the measuring cylinders, on daily basis for 7 days and thereafter weekly for 8 weeks.
The sedimentation volume was calculated using the formula:

$$F = Vu / Vo \times 100 \quad \text{----------►} \quad \text{Equation (1).}$$

Where, Vu = ultimate volume of sediment and Vo = original volume of sediment before settling occurred. Graphs of sedimentation volume were plotted against time.

Rheological assessment:
Viscosities of the prepared suspensions were determined using a Brookfield DV I prime digital viscometer. The guard leg and spindle were inserted into the fluid medium and the viscometer was run at different speeds of 20, 30, 50, 60 and 100 r.p.m. at room temperature. Viscosity values were recorded for different speeds of rotation. Graphs of viscosity versus speed of rotation were plotted.

Assay of Cefixime for Oral Suspension:
The Cefixime trihydrate determined using HPLC Shimadzu, Model: Prominence, LC 20 AB
and methods described in U.S. Pharmacopeia National Formulary 32.

FT-IR spectroscopy:
The IR spectra of Cefixime trihydrate pure material and Cefixime marketed product were recorded from 400 to 4000 cm-1 on FT-IR spectrophotometer IR Affinity Shimadzu by using method described in (BP2014).

RESULTS AND DISCUSSION

Table 1: Representative Formula of Cefixime trihydrate 100 mg/5 ml for Oral Suspension

No.	Ingredients	Weight per unit (gm)	Purpose [16]
1	Cefixime trihydrate	0.600	Active
2	Sodium benzoate	0.060	Preservative agent
3	Strawberry flavor	0.150	Flavouring agent
4	Sucrose	13.920	Sweeting agent/Diluent
5	Areosil	0.150	Glidant
6	Anogeissus Leiocarpus gum	0.120	Suspending agent
Total		**15.000**	

Comparison with marketed preparation:
In-vitro of representative formula of Cefixime trihydrate and marketed preparation were compared as follows.

pH measurement:
Table 2 show insignificant difference in pH, the pH ranged between 3.77 to 3.68 in representative formula of Cefixime trihydrate, and 3.82 to 3.71 in marketed preparation, there is no significant change of pH in the prepared formulation in comparison with marketed product shows good stability for 7 days.

Table 2: pH of Formula of Cefixime trihydrate and marketed preparation at 25°C

#	pH of the formulation at 25°C	pH of marketed preparation at 25°C
Day 1	3.77	3.82
Day 7	3.68	3.71

Specific gravity at 25°C:
Table 3 shows that the specific gravity in day one to day seven, ranged between 1.45 to 1.43 in representative formula of Cefixime trihydrate, and 1.4 to 1.39 in marketed preparation, also there is no significant change of specific gravity in the prepared formulation in comparison with marketed product during 7 days.

Table 3 : Specific gravity of formula of Cefixime trihydrate and marketed preparation at 25°C.

#	Specific gravity of the formulation at 25°C.	Density and specific gravity of marketed preparation at 25°C
Day 1	1.45	1.40
Day 7	1.43	1.39

Sedimentation volume and rates:
Figure 2 shows that the sedimentation volume of cefixime trihydrate and marketed product respectively is 0.8-0.7 and 0.83 – 0.71 after 28 days. The shape of the curve shows good stability of formulated of Cefixime trihydrate suspension.

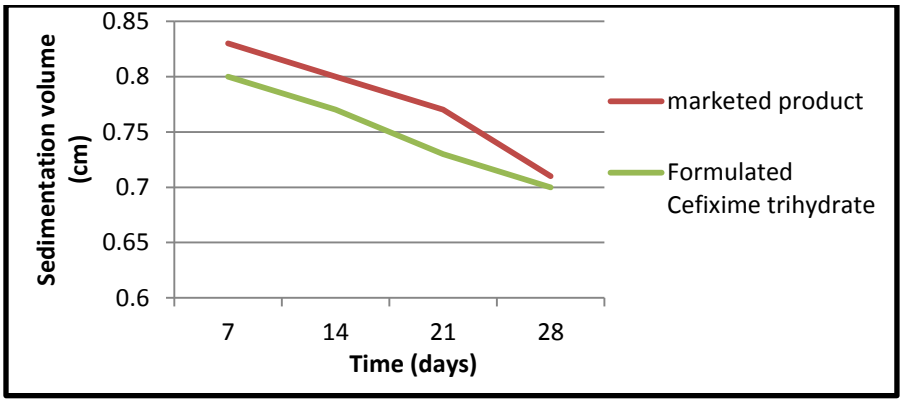


Figure 2: Variation of sedimentation volume of Cefixime trihydrate oral suspension in Anogeissus leiocarpus gum in comparison with marketed product.

Rheological assessment:

Figure 3 shows the rheological properties of suspensions to investigate the relationship between viscosity and suspendability using viscosity of suspensions offers the advantage of slower sedimentation; however [13,14], it may compromise other desirable properties for oral suspensions, and ease of administration. The property of shear thinning is highly desirable so that the suspension is highly viscous during storage when minimal shear is present so that the sedimentation rate is slow and has low viscosity for oral suspension (high shear) facilitate ease of pourability [15].

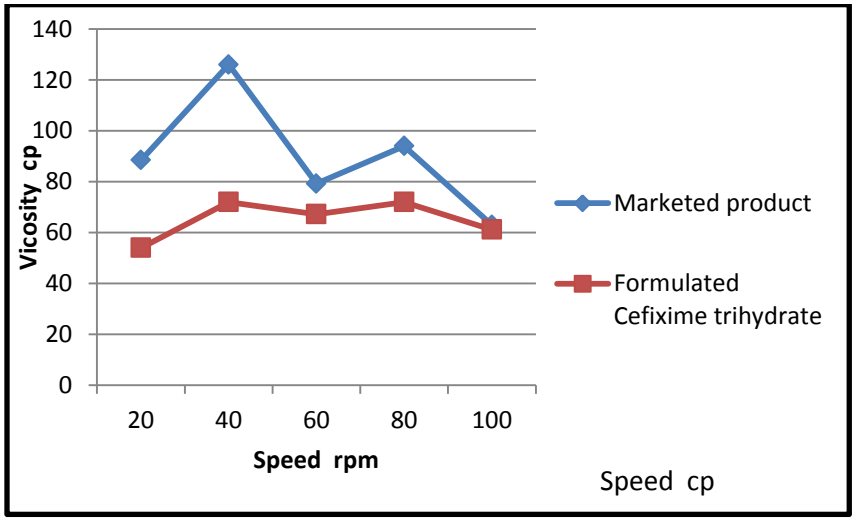
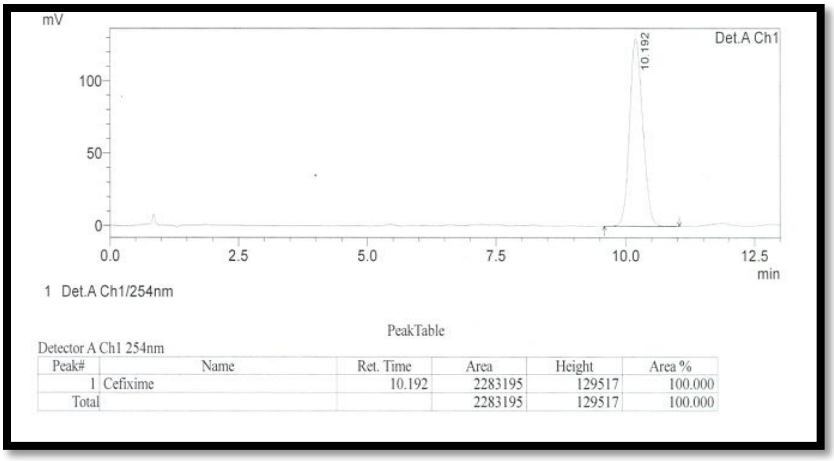


Figure 3: Variation of viscosity with speed of Cefixime oral suspension formulated with *Anogeissus leiocarpus* gum.

Assay for Cefixime for Oral Suspension:

Figure 4 and 5 show the chromatogram of cefixime oral suspension and marketed product, the peak in cefixime formulation and marketed product have indicated elution time indicate absolute similarity of test sample and control sample, the assay for constituents formula of cefixime trihydrate and a marketed product was carried out as per USP 2014, the assay was 100.05% - 92.41% for formula of cefixime trihydrate, and 110.6% – 103.30% for the marketed product respectively, it was in good agreement with the label claim during the 5 days at home storage conditions. The assay test in the constituents' marketed product.

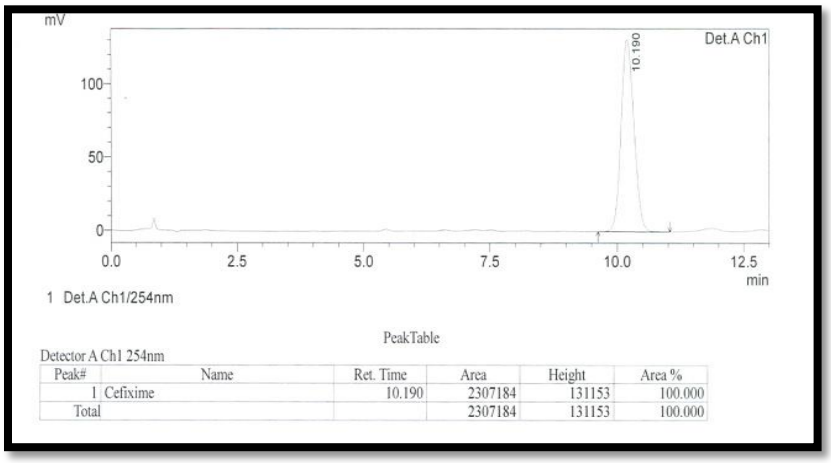


PeakTable

Detector A Ch1 254nm

Peak#	Name	Ret. Time	Area	Height	Area %
1	Cefixime	10.192	2283195	129517	100.000
Total			2283195	129517	100.000

Figure 4: Chromatogram of formulated Cefixime trihydrate.



PeakTable

Detector A Ch1 254nm

Peak#	Name	Ret. Time	Area	Height	Area %
1	Cefixime	10.190	2307184	131153	100.000
Total			2307184	131153	100.000

Figure 5 : Chromatogram of marketed product.

FT-IR Studies:

Figure 6 and 7 show the IR spectrum of formulated Cefixime trihydrate and marketed product respectively, the correlated of cefixime trihydrate and excipients in the region of 3400 – 3500 cm-1 was found due to the N-H (aromatic) stretching. However other peaks related to C-H, C-O and carbonyl stretching remain unchanged. This indicates that overall symmetry of the molecule might not be significantly changed; therefore, the FTIR study revealed that there is no interactions' taking place between Cefixime trihydrate and excepient in formulated product and as similar to that of marketed product.

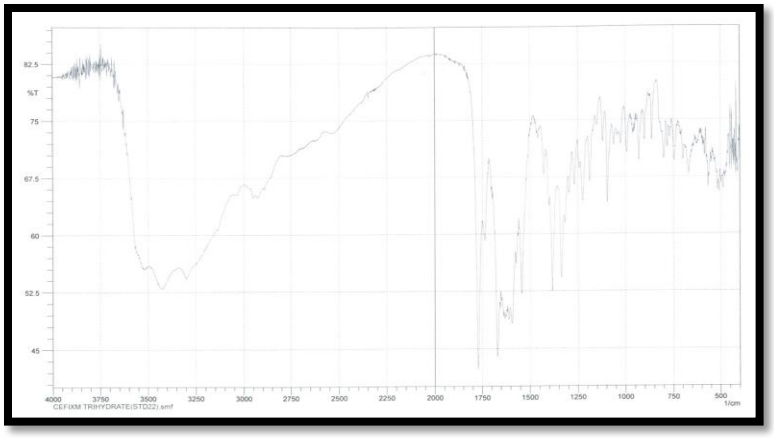


Figure 6 : FTIR spectra of the pure cefixime trihydrate.

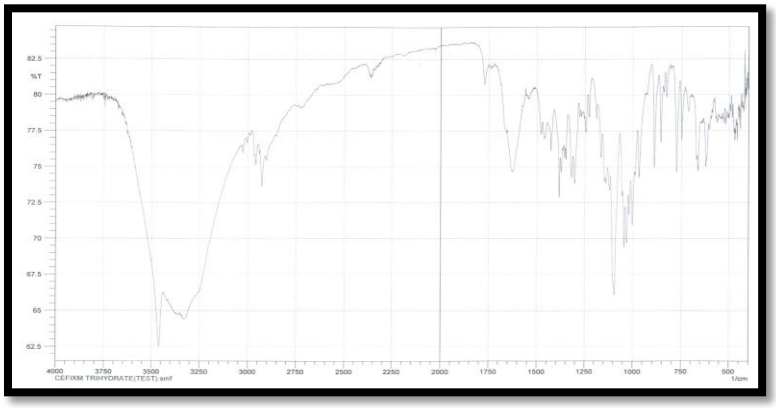


Figure 7: FTIR spectra of the cefixime trihydrate in marketed formula.

CONCLUSION

Formulated Cefixime trihydrate and marketed product show no significant difference in physicochemical properties, evaluated for pH, density, sedimentation, rheological assessment, and also assay.

Gums have wide applications in pharmaceutical industry as tablet binders, suspending agents, filling agents and also in the food industry, cosmetics and in paper and textile industries. Also, it is cheap, and easily available than the synthetic products. On the other hand, the natural excipients are preferred on the synthetic and semi-synthetic ones because of their lack of toxicity, low cost, soothing action, availability, and nonirritant nature of the excipients.It is therefore recommended that the pharmaceutical use of this gum as a close substitute for an official gum like Acacia Senegal (gum Arabic) be exploited in drug formulation.

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REFERENCES

[1] Avari JG; Bhalekar. *Indian drugs*. **2004,** 41, 19-23.
[2] Smolinske; Susan C. Handbook of Food, Drug, and Cosmetic Excipients, CRC press. **1992,** 7.
[3] Cefixime trihydrate, British pharmacopoeia, **2013,** 1, 410-411.
[4] Sean Sweetman. Martindale, Royal Pharmaceutical Society of Great Britain (RPS) Publishing, UK. **2009**

[5] Roche G. Cefixime. The first oral third generation cephalosporins. Presse Med. **1989.**
[6] Indian Drugs, **2003,** 40 (12), 334-336.
[7] Philip Mathews. Advanced Chemistry, Cambridge University Press. **1991.**
[8] David A WillIams; Thomas L Lemke. Foye's Principles of Medicinal Chemistry, 5th edition, Lippincott Williams & Wilkins, Philadelphia, **2002.**
[9] Jaime N Delgado; William A Remers. Text book of organic and medicinal and pharmaceutical chemistry, Wilson and Gisvold's, Philadelphia. **1998.**
[10] Wu DH. Clin Ther. **1993**, 15(6), 1108-19.
[11] Sakane K; Kawabata K; Inamoto Y; Yamanaka H; Takaya T. *Yakugaku Zasshi*. **1993,** 113(9), 605-26.
[12] Memon IA; Billoo AG; Memon HI. *South Med J*. **1997,** 90(12), 1204-7.
[13] Volker Bühler. Generic Drug Formulations, BASF Fine Chemicals. **1998.**
[14] Pritam Dinesh Choudhary; Harshal Ashok Pawar. *Journal of Pharmaceutics*. **2014**, 9.
[15] Alok K. Kulshreshtha; Onkar N. Singh G. Michael Wall. Pharmaceutical Suspensions, Springer. **2010.**