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PREPARATION AND EVALUATIONS OF DIATRIZOATE SODIUM LIQUID ORAL FORMULATION

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ABSTRACT
X-ray diagnostic agents (contrast media) are widely used as adjuncts to diagnostic visualization techniques as they help to illustrate the differences between tissues by introducing them to the area of interest to increase its density and absorption of X-rays. Diatrizoic acid is radio opaque ionic contrast media utilized orally and parentrally for symptomatic purpose. The goal of this investigation is to develop a liquid oral contrast media and evaluate the physicochemical parameter were compared with the changes in accelerated stability testing for the documentation of these plan nearby with FTIR information. Quality of final solution was evaluated with the parameters: pH, iodine iodide test and drug content. Three batches were formulated of the solution. All the batches were evaluated for physicochemical parameters, pH and drug content. The formulated batches under gone stability studies, no turbidity were observed for 60 days studies. All the batches assure the reproducibility and each parameter were complying with specifications.

KEYWORDS: Diatrizoate sodium, oral liquid formulation, contrast media.

1. INTRODUCTION

Diatrizoic acid is a contrast agent used during X-rays. This incorporates when envisioning veins, the urinary framework, spleen, and joints, just as during PC tomography (CT filter). It is controlled by oral, parenteral, and so forth. Diatrizoic acid is an iodinated ionic radiocontrast operator with high osmolality with USP standard medication. [1][2] The IUPAC name of medication is Sodium 3,5-diacetamido-2,4,6-triiodobenzoic acid. It's a fluid oral detailing containing one or more active ingredients in a suitable vehicle; they may in some cases consist simply of a liquid active ingredient used as such.[3] The reason for this examination is that to archived the plan based documentation and with strategy for arrangement and their assessment parameters. The motivation behind this investigation is that to reported the definition based documentation and with strategy for planning and their assessment parameters. By the solvency, stability, drug content (assay) and FT-IR study.[4]

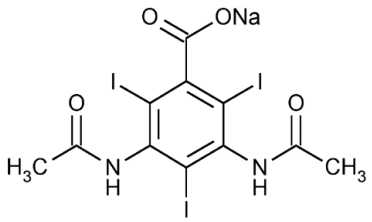


Figure 1: Structure of Diatrizoic Acid.

2. Experimental Work[5]

2.1 Formulation of Diatrizoic Acid

The ingredients utilized for plan depends on mechanical cluster producing record (BMR) information, with monetarily acknowledged and utilizing seasoning operator for patients convince.

Table 1: Formulation of Diatrizoic Sodium.

Sr. No.	Ingredient	Uses	Quantity Taken
1.	Diatrizoic Acid USP	Active Ingredient	87.50 g
2.	Sodium Hydroxide	Base	5.42 g
3.	Sodium Citrate	Acidity Regulator	0.50 g
4.	Disodium EDTA	Chelating agent/ Stabilizer	90.02 g
5.	Methyl Paraben	Preservative	q.s.

6.	Sodium Saccharin	Sweeting Agent	q.s.
7.	Pineapple Flavour	Flavoring Agent	q.s.
8.	Distilled Water	Vehicle	q.s.

Diatrizoate Sodium Solution 30 ml container (Batch of 3 Container). The total volume formulated 200 ml. The concentration of Diatriozic Acid drug was 41.7 % w/v.
Above prepared formulation was transfer into 3 holder containing 30 ml each in compartment for the solidness investigation and item condition during dependability and contrasted and the advertised detailing information for documentation. Preparation are mark as F1, F2, and F3 separately and evaluate individually in all evaluation parameters.
F: Formulation

Method of Preparation
Mixing the half amount of water for 600-800 rpm and include precisely gauge sodium hydroxide and water and get ready basic media and mix it for 5-10 min, at that point disodium EDTA and sodium citrate mix delicately, gradually they are solvent in water at that point include gauge measure of Diatrizoic acid and mix, Check the pH and alter upto 6.5-7.5 by utilizing NaOH solution. The above fixing are totally solvent in water. Include remaining fixing methyl paraben and sodium saccharine with pineapple flavoring agent, make the last volume with DM water. An unmistakable straightforward arrangement is. Fill the arrangement in the appropriate compartment for additional method.

2.2 Marketed Preparation as Control Batch
Marketed Formulation utilized as Control Batch with the Formulated cluster for particularity and correlation study Diatrizoate Sodium arrangement with their assessment parameter study and their outcome.

Table 2: Marketed Formulation Details.

Brand Name	Gastrovideo
Chemical Name	Diatriozate Sodium USP Solution 30 ml
Composition	Datrizoate Sodium USP – 41.7 % w/v In flavoured aqueous based – q.s. (Iodine Content – 249.64mg/ml)
Manufactured By	Unijules Life Sciences Ltd.

2.3 Stability and Storage
Formulation of Diatrizoate Sodium was formulated and kept for stability study for 60 days in temp 40°C±65% alongside with control batch sample.

2.4 Evaluations parameters[6][7]
A) Identification Test
Heat about 500 mg in a suitable crucible: violet vapors are evolved.

B) pH
Placed an accurately measured amount 2 - 5 ml of the optimized formulation a 100 ml volumetric flask and made up the volume up to 100 ml with distilled water. pH was measured with the help of digital pH meter.

C) Assay
Transfer about 400 mg of Diatrizoic Acid, accurately weighed, to a glass-stoppered, 125-mL conical flask, add 30 mL of 1.25 N sodium hydroxide and 500 mg of powdered zinc, connect the flask to a reflux condenser, and reflux the mixture for 1 hour. Cool the flask to room temperature, rinse the condenser with 20 mL of water, disconnect the flask from the condenser, and filter the mixture. Rinse the flask and the filter thoroughly, adding the rinsings to the filtrate. Add 5 mL of glacial acetic acid and 1 mL of tetrabromophenolphthalein ethyl ester TS, and titrate with 0.05 N silver nitrate VS until the yellow precipitate just turns green. Each mL of 0.05 N silver nitrate is equivalent to 10.60 mg of $C_{11}H_9I_3N_2O_4 \cdot C_7H_{17}NO_5$.

D) Iodine Iodide Test
Test preparation - Transfer 2.0 g to a 50-mL centrifuge tube provided with a stopper, dilute with water to 24 mL, and shake to dissolve.
Procedure - Add 5 mL of toluene and 5 mL of 2 N sulfuric acid, shake, and centrifuge: the toluene layer shows no red color. Add 1 mL of sodium nitrite solution (1 in 50), shake, and centrifuge: any red color in the toluene layer is not darker than that obtained when a mixture of 2.0 mL of potassium iodide solution (1 in 4000) and 22 mL of water is substituted for the solution under test (0.02% of iodide).

E) Thin Layer Chromatography
It responds to the Thin-Layer Chromatographic Identification Test, the test solution and the Standard solution being prepared at a concentration of 1 mg per mL in a 0.8 in 1000 solution of sodium hydroxide in methanol, the solvent mixture being a mixture of chloroform, methanol, and ammonium hydroxide (20:10:2), and short-wavelength UV light being used to locate the spots.

2.5 Evaluation of Formulation for Stability[8-11]
For a product to be stable, it should be within the limit of monograph of specification, regarding its identity, strength, quality and purity throughout its shelf life. The purpose of stability testing is to provide evidence on how the quality of drug substance or product varies with time under the influence of variety of the environmental factor like temperature, humidity, light etc. thus enabling recommendation of storage condition and to establish shelf life. In stress testing of a drug or a product it is exposed to elevated temperature and humidity, over a period of time, called the "accelerated stability

condition" and the data obtained predicts stability, storage condition and shelf life of drug substance or product when kept under specified storage condition. The prepared formulation was subjected to accelerated stability study at 40℃±65% for a period ranging from 1st day to 60 days.

The formulation was tested for

A) Identification
B) pH
C) Iodine Iodide
D) % content (Assay)

2.5 Drug-Excipient Interaction Study

After the selection of emulsifiers all the formulation ingredients were subjected to drug excipient interaction studies to determine any possible interaction with drug molecule. The interaction study was carried by using Fourier Transform Infra-red spectroscopy (FTIR).

2.6 Fourier Transform Infrared Spectroscopy (FT-IR)[12]

The FT-IR spectra were obtained using FT-IR spectrometer (Shimadzu).The samples (Diatrizoic acid/Excipient) were previously ground and mixed thoroughly with potassium bromide, an infrared transparent matrix in 1:5 (sample : KBr) ratio, respectively. The KBr discs were prepared by compressing the powders at a pressure of 5 tons for 5 min in a hydraulic press. Thirty scans were obtained at a resolution of 2 cm^{-1} from 4500 to 400 cm^{-1}.

3. RESULTS AND DISCUSSION

3.3 Test Result

Table 3: Identification.

Sr. No.	Formulation	Identification
1	Control batch	Complies
2	F1	Complies
3	F2	Complies
4	F3	Complies

In the above table showing that Diatrizoate sodium shows colour test complies.

Table 4: pH of formulation.

Sr. No.	Formulation	pH (6.5-7.5)
1	Control batch	7.2
2	F1	6.9
3	F2	6.9
4	F3	6.9

pH of all formulation was found in the range of 6.5-7.5. Ideally, the formulation should have possessed the pH in range 6.5-7.5 so as to minimize discomfort and irritation to the body. No modification of pH was attempted for the experimental formulation for the reason of solubility and stability.

Table 5: Assay.

Sr. No.	Formulation	Assay (95.0-105.0%)
1	Control batch	98.27 %
2	F1	98.21%
3	F2	97.81%
4	F3	96.80%

From the table it was clear that the % purity of Diatrizoate Sodium Formulation is within the range.

Table 6: Iodine-Iodine Test.

Sr. No.	Formulation	Test Result
1	Control Batch	Complies
2	F1	Complies
3	F2	Complies
4	F3	Complies

As there was no red colour in the toluene layer hence the above formulation complies the test.

Table 7: Rf values of formulation.

Sr. No.	Formulation	Rf Value (Less Than 1)
1	Control batch	0.80
2	F1	0.75
3	F2	0.72
4	F3	0.69

As the Retention factor was less than 1 it indicates that the above formulation do not content impurities.

3.4 Stability Results

Table 9: Particulate matter.

Sr. No.	Formulation	Particulate Matter	
		1st day	60th day
1	Control batch	Transparent	Transparent
2	F1	Transparent	Transparent
3	F2	Transparent	Transparent
4	F3	Transparent	Transparent

Table 10: Assay.

Sr. No.	Formulation	Assay %w/v	
		1st Day	60th Day
1	Control batch	97.21	97.19
2	F1	97.41	97.11
3	F2	97.51	97.05
4	F3	98.02	97.21

Table 11: pH.

Sr. No.	Formulation	pH	
		1st Day	60th Day
1	Control batch	7.2	6.9
2	F1	6.8	6.5
3	F2	7.1	6.6
4	F3	6.9	6.7

3.5 Drug Excipient Interaction Study

The communication study was conveyed by utilizing Fourier Transform Infrared spectroscopy (FTIR). Similarity concentrate by Fourier changes infrared spectroscopy (FT-IR). Appeared in figure, FTIR are the

assimilation Spectrum of A) Diatrizoic acid B) 1:1 Physical mixture of Diatrizoic acid and Sodium Hydroxide, C) 1:1 Physical mixture of Diatrizoic acid and Sodium citrate, D) 1:1 Physical mixture of Diatrizoic acid and Disodium EDTA, E) 1:1 Physical mixture of Diatrizoic acid and mixture of all excipient. In order to characterize possible interactions between the drug and the excipient, infrared spectra were recorded. Infrared spectrum of Diatrizoic acid is characterized by the aromatic-0H in plane bend at 1451 cm^{-1}, COOH group stretching at 1540 cm^{-1}, aromatic nitro compounds at 1465 cm^{1}. Looking at the spectra of Physical mixtures of different excipient separately lastly with blend of all excipient with that of Diatrizoic acid gives thought regarding conceivable communication. No any noteworthy move in assimilation groups (which are qualities of Diatrizoic acid) was watched. In this manner it very well may be learned that no noteworthy association in the Diatrizoic acid and excipient exists.

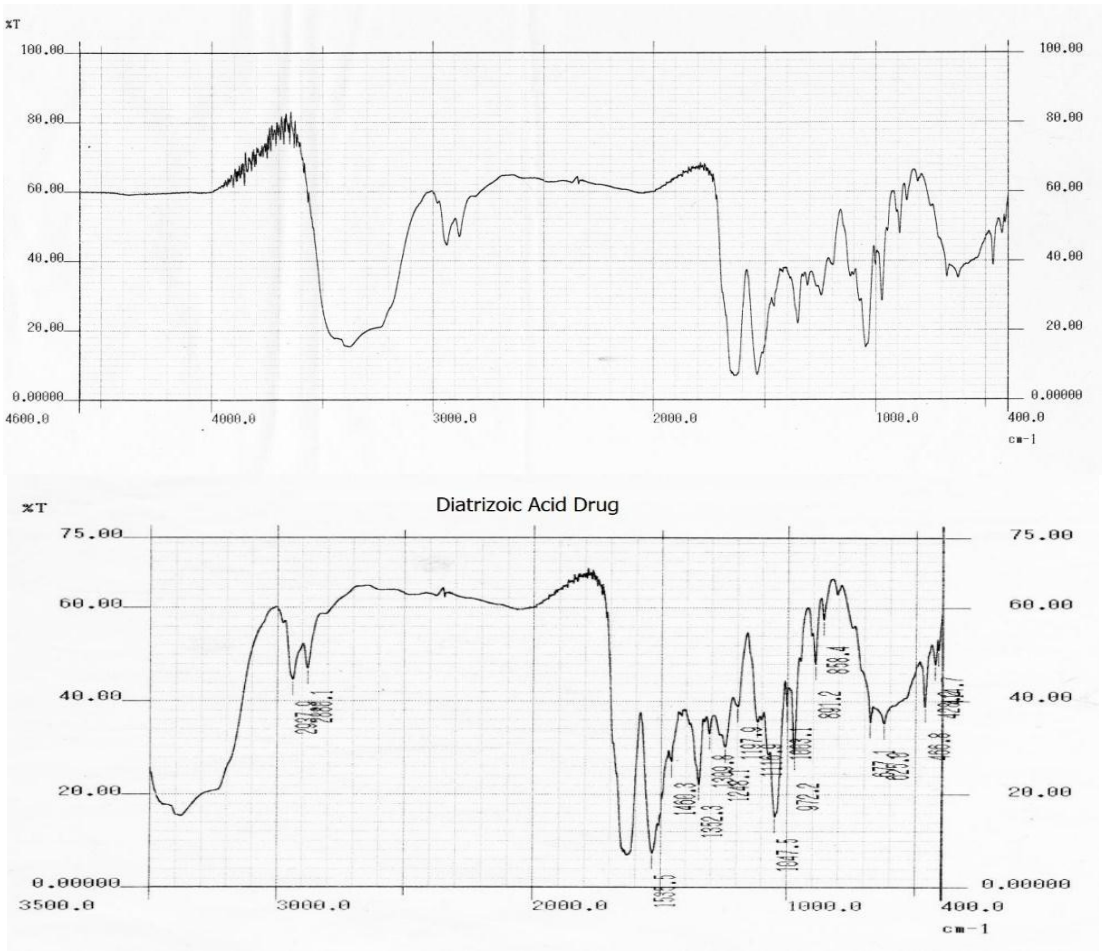
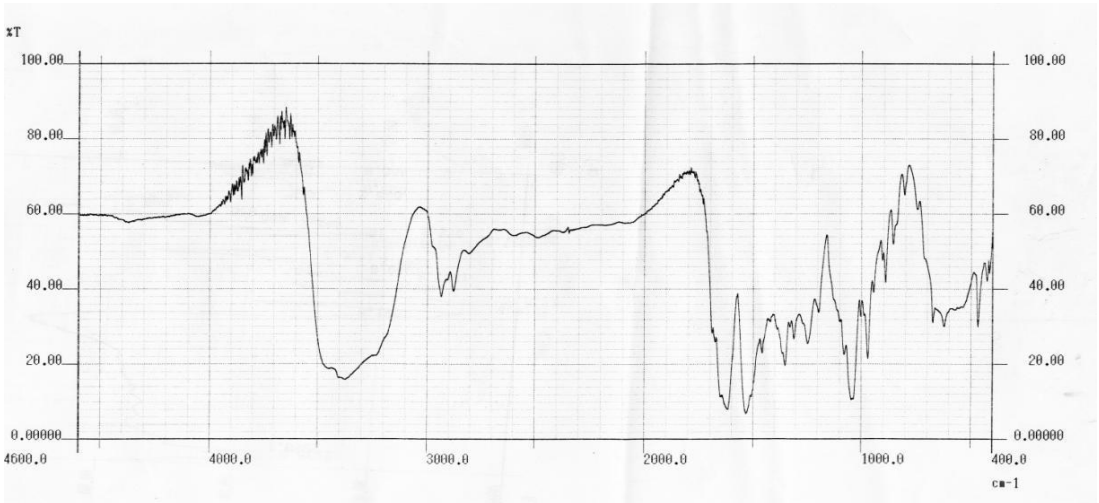


Figure 2 A: FTIR spectrum of Diatrizoic acid drug.



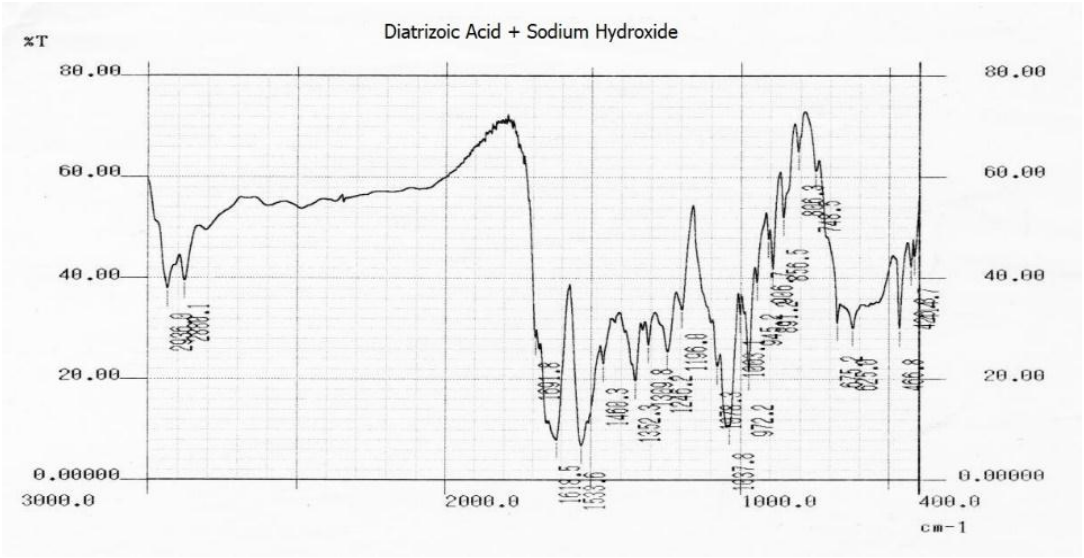
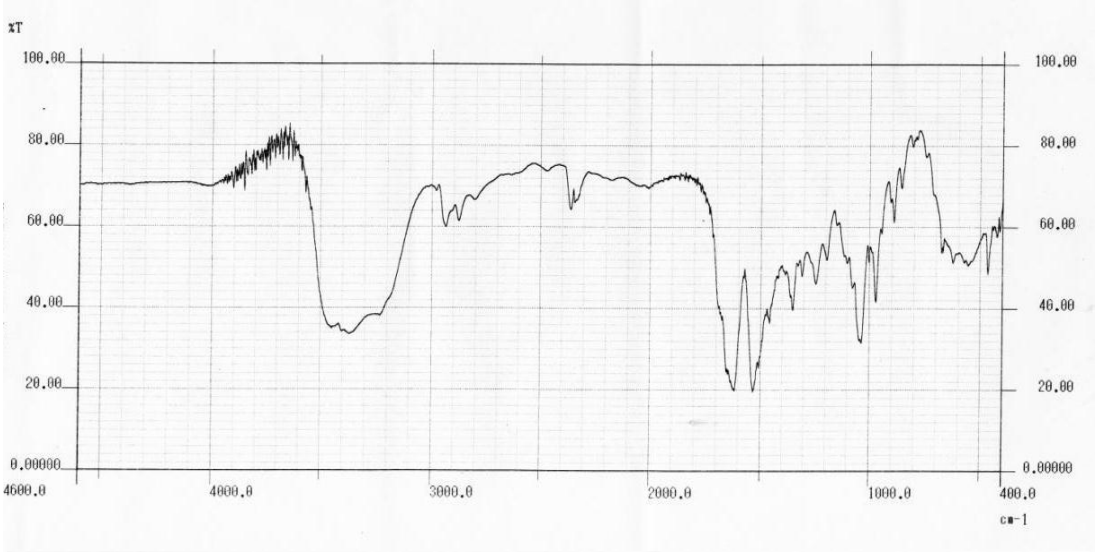


Figure 2 B: FTIR spectrum of Diatrizoic Acid + Sodium Hydroxide.



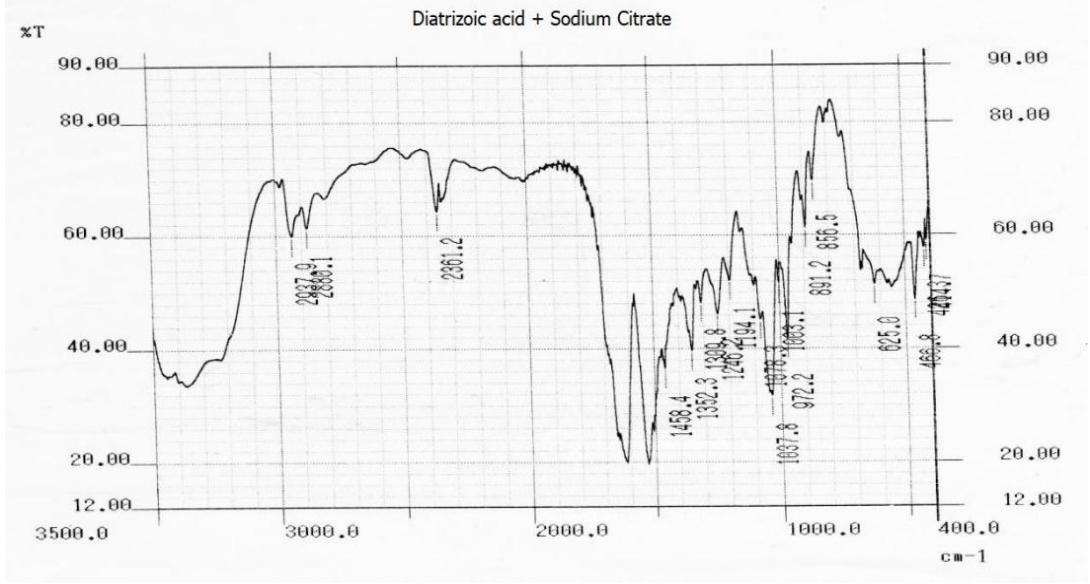


Figure C: FTIR spectrum of Diatrizoic Acid + Sodium Citrate.

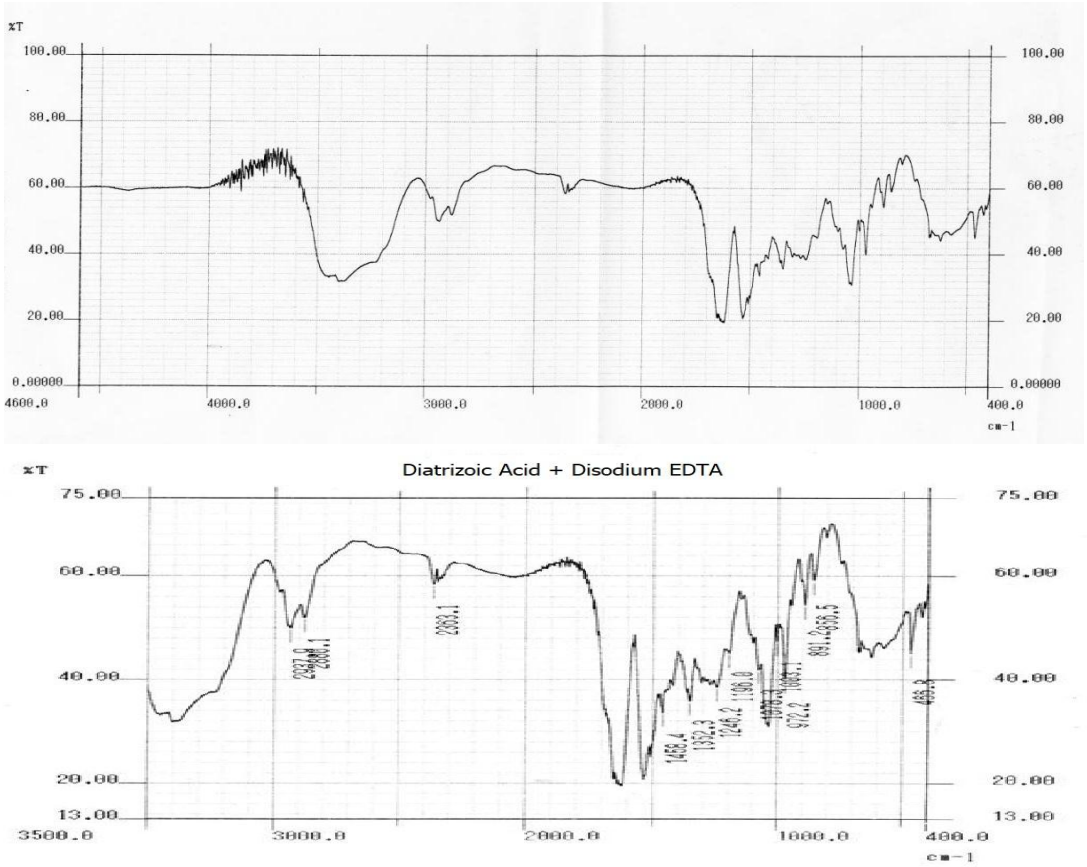


Figure D: FTIR spectrum of Diatrizoic Acid + Disodium EDTA.

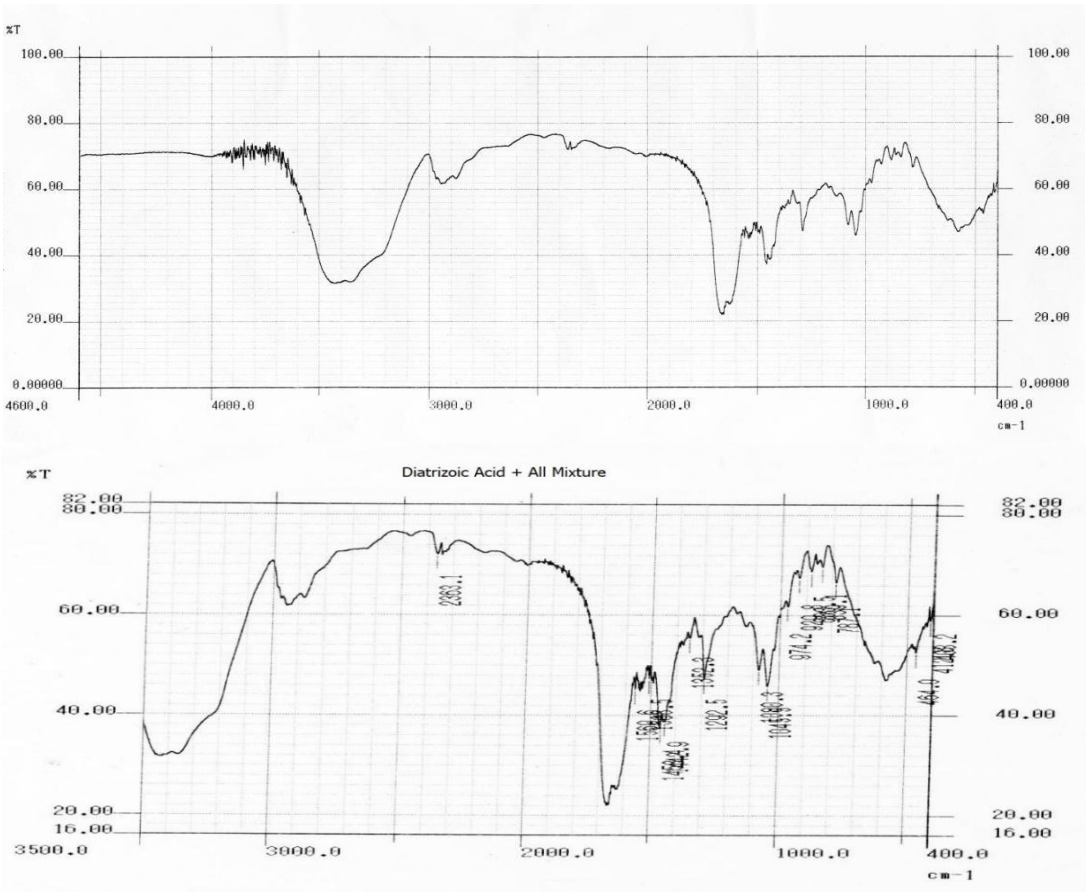


Figure E: FTIR spectrum of Diatrizoic Acid + All Mixtures.

4. CONCLUSION

The oral formulation of diatrizoic acid using desired ingredient provide a better alternative for increasing stability of formulation. diatrizoic acid is a radio opaque ionic contrast media, having limited solubility in water.

In the present work the oral formulation of diatrizoic acid was formulated by using desired ingredient and solubility enhancers. Stability studies of formulation at 40°C±65% for two months showed no significant effect on physical properties and assay. No subtle variation in infrared absorption patterns FTIR study, it can be concluded that no significant drug excipients interaction exists.

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