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Effect on Binary & Ternary Inclusion of Ibuprofen & Different Amino Acid Complex on Phase Solubility

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ABSTRACT

The aim of present research was to formulate and characterize inclusion complexes between β-cyclodextrin (β-CD) and Ibuprofen. Equimolar/ β-CD solid system in the presence and absence of 0.2% (w/v) β-CD was prepared. A phase solubility study was done to estimate solubility constant (KS) and complexation efficiency (CE). Improvement of KS and CE showed the additive effect of auxiliary substances (β-CD). The dissolution properties of binary and ternary systems were determined and compared with alone. The ternary system has shown several times faster than the binary system of Ibuprofen. The optimized binary and ternary systems were characterized by phase solubility. These results showed that ternary inclusion complexes were formed.

KEYWORDS: *Ibuprofen, β-cyclodextrin leucine, glycine, Stability constant*

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INTRODUCTION

Ibuprofen is a poorly water-soluble drug. The aim of this study was to determine whether inclusion complexes betweenβ-cyclodextrin (βCD) and Ibuprofen are formed and also studied effect of auxiliary substance on Ibuprofen. The aim of present research was to formulate and characterize inclusion complexes between β-cyclodextrin (β-CD) and Ibuprofen. Equimolar Ibuprofen/ β-CD solid system in the presence and absence of 0.2% (w/v). A phase solubility study was done to estimate solubility constant (KS) and complexation efficiency (CE). Improvement of KS and CE showed the additive effect of auxiliary substances (β-CD). The dissolution properties of binary and ternary systems were determined and compared with Ibuprofen alone. The ternary system has shown several times faster than the binary system of Ibuprofen. The optimized binary and ternary systems were characterized by phase solubility. These results showed that ternary inclusion complexes were formed.

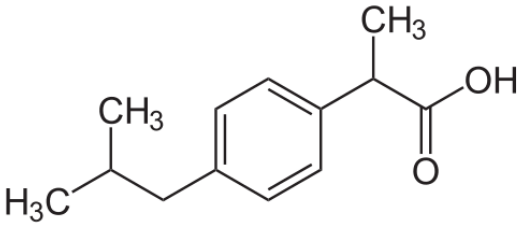
The present study is intended to evaluate the possibilities to improve ibuprofen an oral NSAID drug - solubility in water, based on inclusion complexes formation with β-cyclodextrin (β-CD),), respectively, and also to estimate their composition and apparent stability constants, Kst, from the phase-solubility diagrams. We have noticed that the phase solubility diagram for the repaglinide – HP-β-CD inclusion complex is A type. Ability of the Ibuprofen to form inclusion complexes with a variety of organic compounds is based on their ability to provide a hydrophobic cavity in aqueous solution for a hydrophobic guest molecule. Ibuprofen served as a versatile carrier for poorly water soluble drugs increasing its solubility and dissolution rate through the formation of inclusion complex. They are capable of alleviating the undesirable properties of drug molecule through the formation of inclusion complex. Hydroxylpropyl-betacyclodextrin is mainly selected for its higher solubility and this generally results in

more extensive solubilization ability towards lipophilic molecule, with good safety.

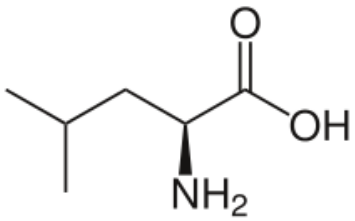
DRUG PROFILE-

Ibuprofen is a medication in the nonsteroidal anti-inflammatory drug (NSAID) class that is used for treating pain, fever, and inflammation. This includes painful menstrual periods, migraines, and rheumatoid arthritis. About 60% of people improve with any given NSAID, and it is recommended that if one does not work then another should be tried. It may also be used to close a patient ductus arteriosus in a premature baby. It can be used by mouth or intravenously. It typically begins working within an hour. it works by inhibiting the production of prostaglandins by decreasing the activity of the enzyme cyclooxygenase. Ibuprofen might be a weaker anti-inflammatory than other NSAIDs.

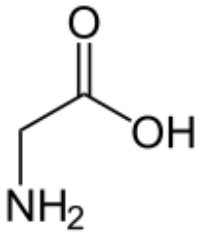
Structure:



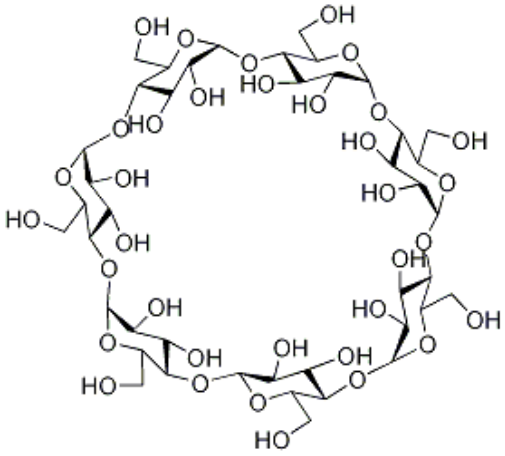
Ibuprofen



Leucine



Glycine



Betacyclodextrin

MATERIALS AND METHODS

CHEMICAL-

0.1n NaOH, Ibuprofen, Beta-Cyclodextren, Glycine, Leucin

Sr. No	Name of equipment
1	Electron weighing balance
2	U.V. visible spectrometer
3	Electronic shaking machine

METHODS

Phase solubility

Phase solubility studies were performed according to the method reported by Higuchi Connors. An excess amount of Ibuprofen was added to 10 ml distilled water containing various concentrations of β-CD (0-0.1 M) within stopper tubes and mixture were shaken for 24Hrs 37±0.5□ at 150 rpm. After achieving equilibrium the solution was filtered through 0.45µm membrane filter paper. The sample was diluted suitably and assayed for content Ibuprofen by U.V. Spectrophotometer at 232 nm .The solubility constant and complexation efficiency was calculated by using the following equations.

$$Ks=\frac{Slope}{So(1-Slope)}$$

Ks=Stability constant

So=solubility of Ibuproefnin absence of CD

$$CE=\frac{Slope}{(1-Slope)}$$

CE=Complexation Efficiency

Aqueous solubility

An excess amount of prepared binary and ternary complex added into 10ml water in stopper tubes. They were kept and shaking to achieve equilibrium appropriate aliquots was withdrawn filtered through What man filter paper no.41.The filtrate analysedspectro photo metrically 232nm**.**

RESULT AND DISCUSSION:

Calibration curve of Ibuprofen-

Conc	Abs
0.2	0.167
0.4	0.402
0.6	0.562
0.8	0.692
1	0.927

Table no.1 Absorbance

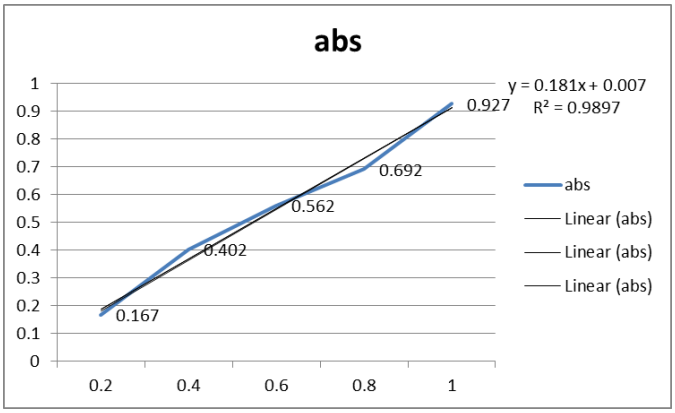


Fig-1.Calibration graph of ibuprofen

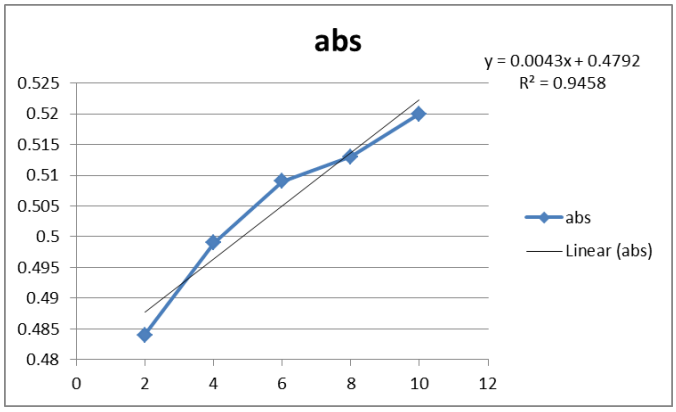


Fig no -3.Ternary inclusion graph for leucine

BINARY INCLUSION GRAPHS-

Conc.	Abs.
0.002	128
0.004	0.284
0.006	0.388
0.008	0.528
0.01	0.686

Table no 2. Absorbance

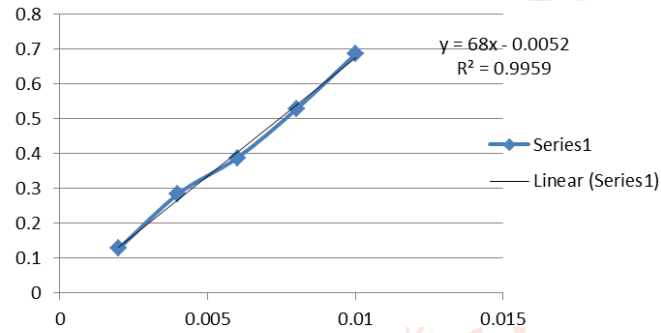


Fig no- 2.Binary inclusion graph

TERNARY INCLUSION GRAPH FOR LEUCINE-

Conc	Abs
2	0.484
4	0.499
6	0.509
8	0.513
10	0.52

Table no 3.Absorbance

TERNARY INCLUSION GRAPH FOR GLYCINE-

Conc	Abs
2	0.528
4	0.533
6	0.535
8	0.537
10	0.539

Table no- 4.Abs. of ternary inclusion of glycin

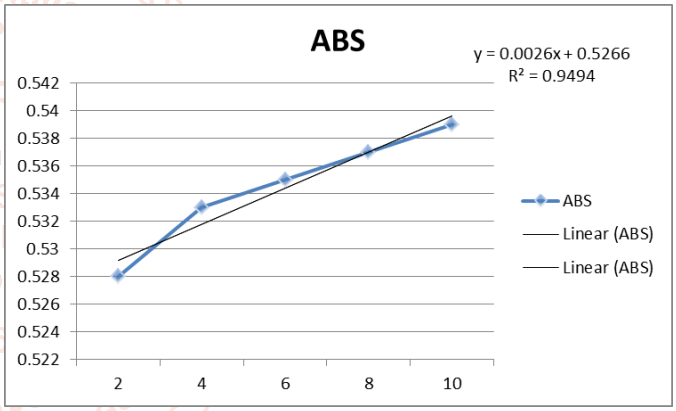


Fig no- 4. Ternary inclusion graph for glycine

Effect of polymer, Leucine on slope of phase solubility diagrams and stability constant (Ks) for binary and tertiary system of Ibuprofen with β-CD-

Systems	Slope	R^2	Ks(M^{-1}) Mean±SD	Kts/Kbs	C.E.
Ibuprofen-β-CD	68	0.995	95.765	95.765	1.01
Ibuprofen-β-CD-Leucine	0.002	0.945	98.764	2.999	0.002
Ibuprofen-β-CD Glycine	0.004	0.949	99.865	1.101	0.004

Table no- 5. Binary and ternary complex phase solublity

Kts/Kbs ratio of Ks for ternary and binary complexes; indicates mean of three readings; S.D.: Standard deviation. P value compared to Ibuprofen-β-CD i.e. significant C.E.: Complexation efficiency.

CONCLUSION:

This study has revealed that the improving the dissolution performance of Ibuprofen by its complexation with β-CD in presence of Leucine. Leucine showed a more pronounced effect on the enhancement of aqueous solubility and faster rate

than binary complex. Phase solubility study of binary and tertiary systems shows that stability constant of ternary system is higher than that of binary system. Thus, addition of Leucine in tertiary complexes of β-CD beneficial in terms of improvement in CE, Rate of complex formation and enhancement of poorly water-soluble Ibuprofen. Ternary complex system was also found to give faster drug release as compared to pure Ibuprofen

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