

# ORAL ABSORPTION ENHANCEMENT OF METFORMIN HCL BY USING PIPERINE

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## ABSTRACT

Metformin hydrochloride is a biguanide, which is used as an oral hypoglycemic agent. It is prescribed as an antidiabetic agent specifically for type-2 diabetes mellitus. Metformin hydrochloride has poor absorption when given orally is 50-60%. The present study is to enhance the oral absorption of metformin hydrochloride by using herbal absorption enhancer i.e. piperine. To enhance the absorption of poorly absorbable drugs from intestine. The invitro Non-everted sac modification method is selected for the absorption studies. The absorption studies are conducted for poorly absorbable drug Metformine HCl in the presence of herbal like black pepper (piperine, Showed an increase in intestinal brush border membrane (BBM) fluidity). During the absorption study, the sample from intestinal are collected for every 15 minutes interval and up to 2 hrs at 233nm. The absorbed drug was analysed by using UV-spectrophotometer. By results of all experimental, it is concluded that the piperine enhancing the absorption activity of Metformine Hcl.

**KEY WORDS:** Metformin HCL, Intestine, Invitro Non-everted sac modification method, piperine(black pepper).

## 1. INTRODUCTION

The process of moment of unchanged drug from the site of administration to systemic circulation is known as absorption(Shobha Rani,2002) In the present work, attempt was to enhance the absorption of poorly absorbable drugs(Metformin Hcl) from intestine. The invitro Non-everted sac modification method is selected for the absorption studies. The experimental animal is fasted for 12-24 hrs. 30 cm length of intestine is taken and immersed in buffer solution (saline pH 7.4). The temperature is maintained at  $37 \pm 0.5^\circ\text{C}$ . The intestine is having drug with buffer solution where as out side the intestine plane buffer is taken. Diabetes is a major public health concern where more and more people are falling prey to the disease in both the developed and developing world. Metformin is a hyperglycemic agent which improves glucose tolerance in patients with type -2 diabetes( Ritub,2007), lowering both basal and postprandial plasma glucose. Clinical studies proved a significant reduction in the risk of myocardial infardtion and overall mortality in overweight patients with type-2 diabetes treated with Metformin Hcl which made the drug a cornerstone in the treatment of patients with type-2 diabetes (Flowerlet Mathew,2010).

## 2. EXPERIMENTAL

**Materials:** Natural piperine was extracted from black pepper, Metformin Hcl from drug India.

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**Extraction of piperine from black pepper(ikan,1991):** Grind 25g fresh peppercorns to a fine powder, place in a soxhlet thimble, and extract with 100ml ethanol for 90min. Cool the resulting solution, filter if necessary, concentrated on the rotary evaporator. Keep the water bath below  $60^\circ\text{C}$  during the concentration. Dissolved the residue in 250ml 10% alcoholic KOH. Decant the solution if any residue remains. Cool the solution in ice bath, and add water drop wise(about 30ml will be required) to precipitate the piperine (Grove,2003).

Collect the piperine on a sintered glass funnel, and dry it on the vaccum pump. Recrystallization from acetone: hexane 3:2 will be produced cleaner material.

### Construction of Calibration curve of Metformin Hcl

[S.S-1]100mg of pure Metformin Hcl was dissolved in the 100ml of buffer solution (7.4 pH).[S.S-2]From the stock solution -1, 10ml of solution is taken and it is diluted to the 100ml with buffer solution(7.4pH). From the stock solution-2, 8-18 $\mu\text{g/ml}$  of concentration was prepared with buffer. Measure the concentration in UV - spectrophotometer at 233nm. For this plain buffer is used as a blank solution. All reading and results shows in Table-1. Plot a graph by taking concentration on X-axis and absorption on Y-axis. The curve was linear and obeys Beers lamberts law.. Resultant graph is shown on the Graph-1.



### Non-everted sac modification method

Intestine A and B of 30cm length of overnight fasted goat is taken. In intestine A pure drug (5mg drug is dissolved in 50ml of saline) solution is loaded and it was tied in both the ends. In intestine B drug with piperine is loaded and tied at both the ends. These intestines were dipped into the organ bath and adequate oxygen is provided to the intestine through aerator. samples were collected in every 15 minutes up to 2hrs.

### Sampling Technique

5ml of sample is taken from each intestine at the intervals of 15min. The sample's were pipette out for 2 hrs. Sample are analysed by UV-spectrophotometer.

Collect the samples and analyzed at 233nm and determine the absorbance. The plain buffer (saline pH 7.4) is used as blank solution. From the absorbance calculate the concentration and amount of drug absorbed for both intestine A and B. The results were shown in the Table-2 and 3. A graph was plotted between the absorbed drug on Y-axis and time on X-axis. The resultant graph was shown in the Graph 2 and 3. Compare the results for plain Metformin Hcl and Metformin Hcl with piperine.

### 3. RESULTS

Table-1: Concentration and Absorbance of pure drug

Concentration (µg/ml)	Absorbance
8	0.085
10	0.095
12	0.110
14	0.125
16	0.150
18	0.163

Graph-1: Calibration curve for Metformin

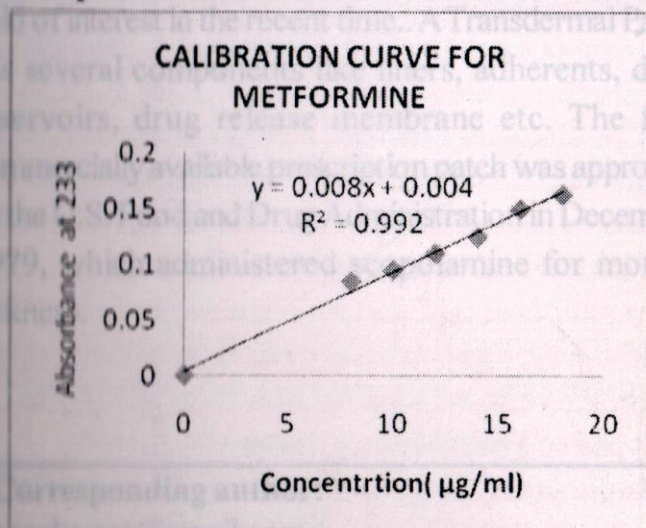


TABLE-2: Absorbance of pure drug (Metformin Hcl)

S.No	Time(min)	Absorbance	Concentration from Graph(µg/ml)	Amount of drug in mg
1	15	0.014	1.5	0.7
2	30	0.022	2.2	1.1
3	45	0.028	3.0	1.5
4	60	0.040	4.2	2.1
5	75	0.048	5.1	2.5
6	90	0.059	6.2	3.1
7	105	0.072	6.6	3.4
8	120	0.072	6.6	3.4

Graph 2:- Amount of drug absorbance

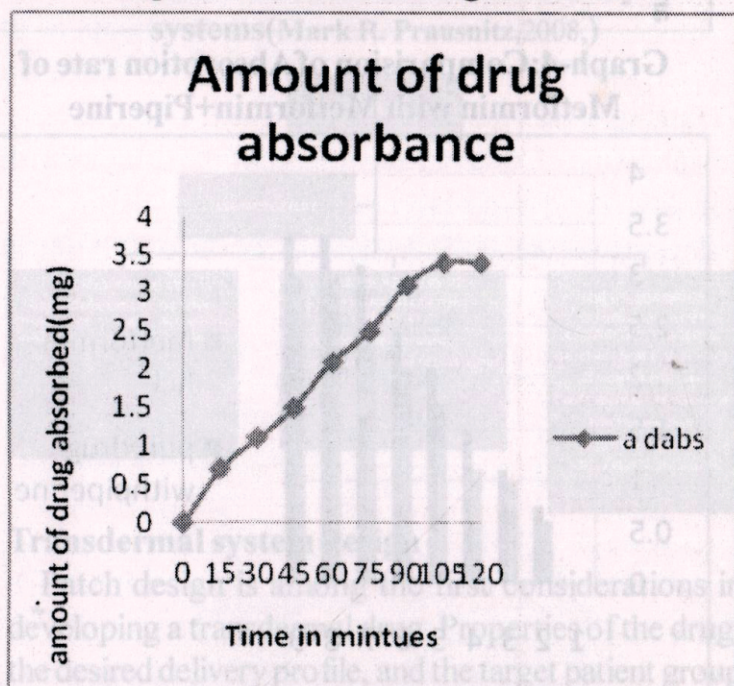
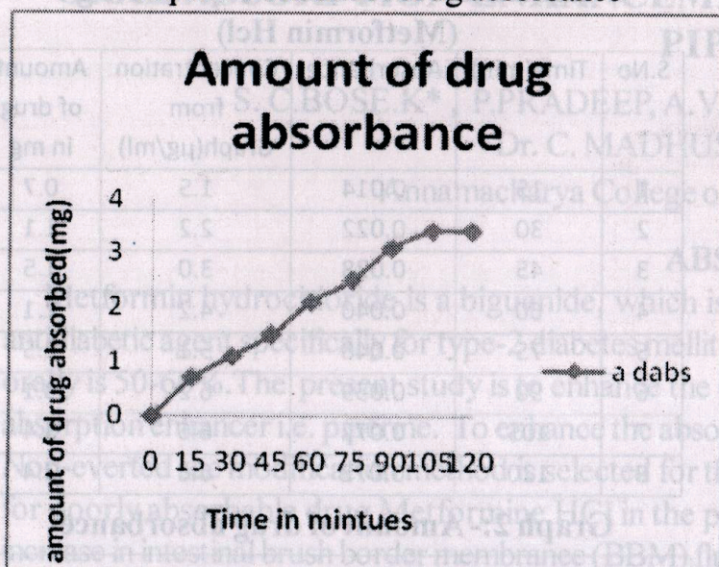


Table3:- Absorbance of drug with piperine

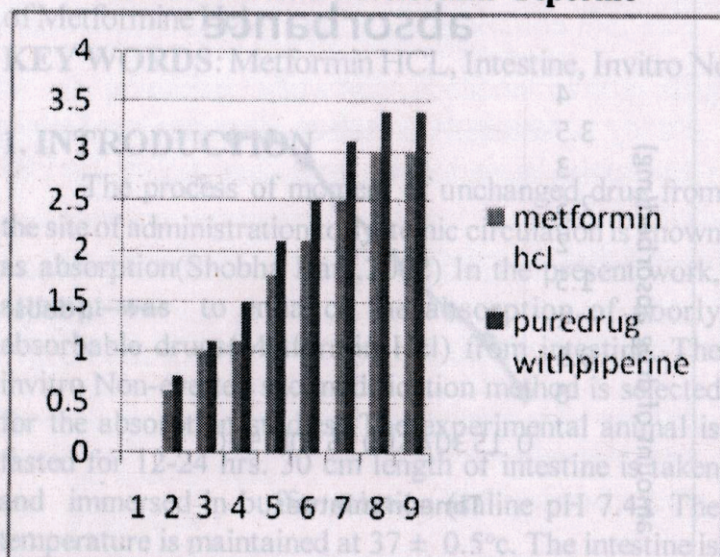
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Graph3:- Amount of drug absorbance



Graph-4: Comparison of Absorption rate of Metformin with Metformin+Piperine



#### 4. CONCLUSION

In the present work attempt was made to enhance the absorption of poorly absorbable drugs from intestine. The invitro Non-everted sac modification method is selected for the absorption studies. The absorption studies are conducted for poorly absorbable drug Metformine HCl in the presence of herbal like black pepper (piperine). During the absorption study, the sample from intestinal are collected for every 15 minutes interval and up to 2hrs. The absorbed drug was analysed by using UV-spectrophotometer.

After analyzing the results of all experimental, it is concluded that the piperine enhancing activity of Metformin HCl.

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