ISSN: 0975-8585

Research Journal of Pharmaceutical, Biological and Chemical Sciences

# Pharmacodynamic Drug Interaction of Metformin with Amla (*Emblica Officnalis*) in Rats

**Sakthivel K*, Senthamarai R, Karpagam Kumara Sundari S and Rajesh C**

Periyar College of Pharmaceutical Sciences, Tiruchirappalli, Tamil Nadu, India

## ABSTRACT

The present study is aimed to explore the pharmacodynamic interaction of metformin with Amla in rats. Wistar albino rats of either sex (160-200 g) were induced diabetes by administering alloxan and they were divided into five groups, each consisting of six rats. Normal control group (1) is treated with 1%w/v carboxy methyl cellulose (CMC) suspension. Group 2 served as diabetic control. To the diabetic 3rd and 4th group Metformin and Amla were administered orally respectively for 7 days. The combinations of Metformin + Amla were administered to the 5th group of diabetic rats for 7 days. On the last day blood samples were collected, and subjected to glucose estimation. . Body weight was also calculated. Metformin significantly reduced the blood glucose level in diabetic rats**.** On the other hand the combination of Metformin + Amla significantly reduced the blood glucose level when compared to Metformin alone. The combination of drugs also increased the body weight of diabetic animals. The herbal drug Amla enhanced the hypoglycemic activity of Metformin due to Pharmacodynamic interactions.

**Keywords**: Amla, Metformin, Pharmacodynamic, Drug-Herb interaction, Diabetes.

***Corresponding author***

ISSN: 0975-8585

## INTRODUCTION

Diabetes is a group of syndromes characterized by hyperglycemia, altered metabolism of lipids, carbohydrates and proteins and an increased risk of complications from vascular diseases. Among diabetics, approximately 95% of patients have type 2 diabetes mellitus (DM), whereas about 5% of patients have type 1 diabetes mellitus (DM). Patients with DM are at risk for microvascular complications like retinopathy, nephropathy and neuropathy and macrovascular complications like myocardial infarction that increase morbidity and mortality [1].

Polypharmacy and multiple drug therapy assume importance in present day clinical practice, since newer molecules are invented everyday and newer challenges face clinicians in managing either a single diseases or simultaneously occurring different diseases. According to one report, the drug interactions may be fourth to sixth leading cause of death in United States [2]. Hence the metabolic drug interaction between drugs is a major concern for the health care professionals and their patients. As per one survey, the incidence of drug-drug interaction range from 3 to 5% in patients taking a few drugs to 20% in patients receiving 10 to 20 drugs [3]. Hence it is necessary to understand and establish such interactions in clinical practice. The clinical observations are very vital in noting the interactions of drugs, but to study the mechanisms of such interactions clinical studies cannot be carried out using human models. Hence animal model studies help in understanding the underlying mechanisms in drug interactions [4]. The present study was intended for studying Pharmacodynamic interactions between Metformin and Amla in rats.

## MATERIALS AND METHODS

Wistar albino rats of either sex were procured from Sri Venkateshwara Enterprises**,** Bangalore**.** Prior approval by institutional ethics committee was obtained for conduction of experiments. The experiment was conducted in the Department of Pharmacology, Periyar College of Pharmaceutical Sciences, Trichy, Tamil Nadu during the period of January-2011. Glucose kit ONETOUCH SELECT manufactured by LIFESCAN, Switzerland, were procured from mediplus health care pharmacy, Trichy, Tamil Nadu. Metformin, were procured as gift sample from MEDO PHARMA Chennai. Amla (amalaki), manufactured by HIMALAYA herbal healthcare was procured from Himalaya heathcare pharmacy Trichy, TamilNadu. Alloxan and CMC were purchased from S.D. Fine Chemicals.

### Animal

Wistar albino rats of either sex weighing 160-200 g were used for the studies. They were fed a standard rat pellet and water *ad libitum*and maintained under standard laboratory conditions. Animals described as fasted were deprived of food for 18 h but had free access to water.

Alloxan induced diabetic rats

The fasted rats were injected with alloxan (150 mg $kg^{-1}$, ip) [5]. One group of six identical rats were kept without alloxan treatment as normal control, group 1. Five days later blood was collected from tail vein under mild ether anesthesia and blood glucose levels were determined. Rats with blood sugar level of 200-350 mg $dL^{-1}$ were considered as diabetic and were employed in the study [6].

The diabetic rats were subdivided into five groups as follows; group 2 (diabetic control) given vehicle (1% W/V CMC); group 3 diabetic rats given metformin (100 mg $kg^{-1}$, orally in 1% W/V CMC); group 4 diabetic rats given Amla (200 mg $kg^{-1}$, orally in 1% W/V CMC); group 5 diabetic rats were given Metformin + Amla (100 mg $kg^{-1}$ , 200 mg $kg^{-1}$orally in 1% W/V CMC). The treatment was given for seven days. In all the groups, the blood sample was collected after 1 h drug treatment and subjected to glucose estimation [7].

**Statistical analysis**

Statistical analysis was done using One Way ANOVA. The combination of Metformin, Amla, and Metformin + Amla was compared with diabetic control. A p-value $< 0.05$ was considered significant.

## RESULTS AND DISCUSSION

The body weight was slightly increased in the normal control rats, whereas in the diabetic rats there was a significant reduction in body weight is due to poor glycemic control and impaired carbohydrate metabolism. Metformin, Amla and in combination of Metformin + Amla treatment significantly prevented this reduction in the body weight of animals in these groups. Although there is a marginal reduction in the body weight of animals in these groups compared to initial body weights it fell short of statistical significant. However the reduction in the body weight was significant when compared to the final weight of normal control rats (Table 1).

Diabetic rats showed increase in serum glucose levels than control. Serum glucose levels showed a reversal near to control values by treatment with Metformin. On the other hand the treatment with Amla slightly decreased the serum glucose level but it lacks statistical significance. Whereas treatment with combination of Metformin + Amla decreased the serum glucose concentration lower than Metformin treatment which is statically significant (Table 1).

In the present study all the drugs increased the body weight of diabetic rats, which was checked on 7th day of treatment. Alloxan treatment decreased the body weight, which is associated with decreased rate of glucose utilization and impaired carbohydrate metabolism. It induces diabetes by destroying $\beta^2$-cells of pancreas and the destruction is almost complete.

ISSN: 0975-8585

**Table 1: Effect of Metformin, Amla and the combination of Metformin + Amla on body weight, Blood glucose**

| Groups | Body Weight (g) | | Blood glucose (mg $dL^{-1}$) |
|---|---|---|---|
| | Initial (0 day) | Final (7 day) | |
| Normal control | 187.3 ± 5.6 | 194.0 ± 5.2 | 95.0 ± 6.2 |
| Diabetic control | 183.2 ± 8.5 | 153.5 ± 3.2 | 323.2 ± 2.2 |
| Amla | 184.6 ± 3.2 | 171.5 ± 3.5 | 208.2 ± 2.6* |
| Metformin | 185.4 ± 2.2 | 172.5 ± 2.3 | 127.5 ± 2.8* |
| Amla + Metformin | 186.7 ± 2.6 | 176.5 ± 4.5 | 103.8 ± 1.9* |

Each Value is mean ± S.E.M of six animals per group. P<0.05 control by One way ANOVA
*p<0.05 Compared to diabetic control

In this study Metformin decreased serum glucose level near to control in diabetic rats after 7 days treatment. On the other hand treatment with combination of drugs such as Metformin + Amla on diabetic rats reduced the blood glucose levels much lower than Metformin treatment. It shows the Pharmacodynamic interaction between Metformin and Amla. This interaction may increase the bioavailability of Metformin and exhibit marked decrease in blood glucose level when compared to Metformin alone. Hence Amla enhanced the Antidiabetic activity of Metformin.

## ACKNOWLEDGMENTS

The authors are grateful to Periyar College of Pharmaceutical Sciences, Tiruchirappalli, Tamil Nadu for providing the necessary facilities to carry out the work.

## REFERENCES

[1] Cerveny JD, RD Leder and CW Weart. Ann Pharmacother 1998;32:896-905.
[2] Yuan R, T Parmelee JD, Balian RS, Uppoor and F Ajayi et al., Clin. Pharmacol. Ther 1999; 66: 9-15
[3] Alan SN and PS Stephen. 1996. Principles of Therapeutics. In: Goodman and Gilman's. The Pharmacological Basis of Therepeutics, 9th Edn., Hardman, J.G. and L.E. Limbard (Eds.). McGraw-Hill, New York, pp: 51.
[4] Satyanarayana S, M Nitin and K Prasad. Indian Drugs 2007;44: 683-688.
[5] Dhawan D, HK Bandhu B, Singh A Singh and JP Nagpal. Indian J Pharmacol 1996;28: 224-226.
[6] Dhanabal SP, CK Kokate M, Ramanathan K, Elango and EP Kumar et al. Indian Drugs 2004; 41: 690-695.
[7] Trinder P. Ann Clin Biochem 1969;6:24-27.