



STUDY OF ANTIMICROBIAL PROPERTY OF METFORMIN

Pharmacology

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ABSTRACT

Metformin is the most widely prescribed first line anti diabetic drug for diabetes worldwide. Antibacterial property had been identified first & intended to treat infections but at the same time it was noticed that metformin "lowered the blood sugar and was non toxic, so that hypoglycaemic effect of metformin became a one of the thrust area of research.

The treatment of microbial infections with anti-microbial drugs became a serious global health issue due to development of antimicrobial drug resistance. In this complexity new drugs related to antibiotic & non antibiotic class or new drug combinations may be the solution against development of resistance in serious microbial infectious diseases. Hypoglycemic, Antihistamines, antipsychotics, Antihypertensive and Local anesthetics had been believed to have powerful antibacterial activity. Hence drugs belongs to respective classes had been grouped together and entitled as "Non- antibiotics". In present study an oral hypoglycaemic drug called metformin antimicrobial activity had been analyzed and the results show that metformin is active against *P. aeruginosa*. Metformin as non-antibiotic antibacterial drug may reduce the morbidity in diabetic patients.

KEYWORDS

Metformin, Non- Antibiotics, Diabetes, Drug resistance

INTRODUCTION

Metformin is believed that marvellous survivor for diabetes and coined as glucose eater among all oral hypoglycaemic agents. In the year 1950 metformin (Fluamine) had been used to treat influenza along with its antibacterial property. Filipino physician, Eusebio Y. Garcia, noted that the metformin "lowered the blood sugar to minimum physiological limit" and was non toxic, so that after 1952 hypoglycaemic effect of metformin became a one of the thrust area of research worldwide. But it is much newer, merely a few centuries old. It belongs to the biguanide class of antidiabetic drug dating from 1920, first used to treat frequent urination and halitosis^{1,2}.

There is an evidence that certain non antibiotics, alone or in combination with conventional & classical antibiotics, may provide better therapeutic management of microbial infections those have association with high risk of resistance to conventional antibiotics³. Drugs like hypoglycemic, antihistamines, antipsychotics, antihypertensive and local anesthetics had been believed to have powerful antibacterial activity. So drugs belongs to these classes have been grouped together and are now entitled as "Non- antibiotics"⁴. Since metformin is used only for the treatment of diabetes, it would have merited sufficient honour but as old hypoglycaemic drug keeps on surprising this medical world with its interesting actions like bacteriostatic, antiviral, antimalarial, antipyretic, analgesic and anticancer. Metformin with these properties can significantly protect humans from tested pathogenic bacteria. Thus it's being beneficial to diabetic patient more than a hypoglycaemic drug^{5,6}. Considering these important properties of metformin present study is planned to analyze the anti microbial property of it by comparing with standard antibiotics like ciprofloxacin & Amikacin.

MATERIALS & METHODS

Bacteria, Media & Method Used

ATCC strains of *Escherichia coli* & *Pseudomonas aeruginosa* were collected from Department of microbiology from a tertiary care teaching hospital. Sterile Muller Hinton agar plates were prepared and used for growth of organisms at optimum conditions.

It was an analytical study with two months of study duration. Assessment of antibacterial activity of metformin had been evaluated by determining the zone of inhibition by disc diffusion method by taking ciprofloxacin & amikacin as standard antibiotic to compare the anti bacterial activity of metformin with two sets of dilutions (100 and 200 µg/10µl) for each drug. The drug concentration had been increased to 300 and 400µg/10µl for further analysis.

Preparation of various concentration of drug

Accurately weighed 5mg, 10mg, 15mg and 20mg of metformin (crude drug) were dissolved in required amount of DMSO and distilled water, since metformin did not dissolve in distilled water with DMSO, thus the same amounts of drugs were dissolved in 0.5ml of methanol to get concentration of 100µg/10µl, 200µg/10µl, 300µg/10µl and 400µg/10µl. The solution of 10µl was dripped onto the disc such that each disc had 100µg, 200µg, 300µg and 400µg of test drug metformin and then the disc was allowed to dry for methanol to evaporate.

Since the Ciprofloxacin (5µg/disc) and Amikacin (30µg/disc) were standard antibiotic agents so the discs with respective concentrations were brought from Hi-media.

Preparation of test inoculums

Sterile muller Hinton agar plates were prepared and incubated at 37°C for 24 hours to check for any contamination. ATCC strains of *E. coli* and *P. aeruginosa* were transferred from the stock cultures onto the MHC plates and were incubated with Sterile filter paper discs (Whatman no. 1) containing drug and placed at appropriate position of the flooded plate surface. The petridishes were incubated at 37°C for 18-24 hours and the diameter of zones of inhibition (mm) was recorded. Similar procedure was followed for ciprofloxacin and amikacin and the cores providing zone diameter was compared to evaluate anti microbial property of metformin.

OBSERVATIONS & RESULTS

Zone of inhibition is taken as the parameter for the assessment of antimicrobial property of selected test drug metformin by dissolving it in methanol. The dilution of metformin in different solvents is summarized in table no 1.

Table 1: Dissolution of metformin for disc preparation

S. no	Solvent	Metformin (crude form) weights	Result of Dissolution
1	Water (5-50ml)	5-50 mg	Not observed
2	DMSO + Water (1+ 49ml)	5-50 mg	Not observed
	DMSO (1ml)	50 mg	Not observed
3	Methanol (0.5ml)	5, 10, 15, 20 mg	Observed 100, 200, 300, 400 (µg /10 µl)

The dissolution of metformin was seen in methanol.

The zone of inhibition is summarized in table no.2. Crude form of metformin as test drug, Ciprofloxacin & Amikacin had been taken as standard antibiotic for comparison of the result. Two sets of two dilutions (100 and 200 µg/10 µl) of metformin was compared with both the standard antibiotics.

Table 2: Zone of inhibition of different drugs by disc diffusion method

S.no	Organism	Test drug concentration (ug/ul) (Metformin)		Standard drug concentration (ug/disc)	
		100µg/10µl	200 µg / 10 µl	Ciprofloxacin (5 µg)	Amikacin (30 µg)
1	Pseudomonas aeruginosa	12mm	15mm	16mm	14mm
2	Escherichia coli	Not seen	Not seen	20mm	16mm

Zone of inhibition is seen with metformin 100 µg/10 µl & 200 µg/10 µl concentrations against Pseudomonas aeruginosa.

DISCUSSION

The antimicrobial property of metformin was reported by many researchers by dissolving it in water & DMSO but the present study observations shows that it did not dissolve in water & DMSO but it dissolved in methanol which may be due to different drug formulations used.

The available literature reported that antimicrobial activity is carried out using the antibiotics which involves the use of antibodies. It is an obvious expectation an antibiotic will always have some antibiotic activity. Since last decade, there has been a tremendous increase in the spread of hyperglycemia & hypoglycemia.

The motive of choosing the “non-antibiotics” class was to know whether the metformin have any antimicrobial activity or not and at what dose and against pseudomonas & E.coli.

Since this was found with such antibacterial and antimicrobial properties. If a hypoglycemic drug contains some antimicrobial activity, that it would be an added advantage for the patient in raise the immunity.

On comparing the results of zone of inhibition among the selected test & standard drugs, metformin was found to have antimicrobial activity but not more than the standard antibiotic drugs that are ciprofloxacin & amikacin. Ciprofloxacin antimicrobial activity when compared with amikacin that was found to be more against the E.coli than Pseudomonas. Metformin was found to have antimicrobial property at a concentration of 100 µg/10ul and also it was slightly increased (12mm-15mm) with the 200µg/10ul of metformin.

The results for the zone of inhibition shows that the standard ciprofloxacin was having almost similar microbial activity (16mm) when compared with the metformin (200 µg /10ul) against to pseudomonas. It was more with ciprofloxacin against E.coli (20mm) and zone of inhibition is not seen with 100 µg/10µl & 200 µg/10ul of metformin against to E.coli. Even after increasing the doses to 300 µg/10 µl & 400 µg/10 µl it was not seen. Metformin found to be more effective against Pseudomonas aeruginosa when compared with the E.coli strains even with the low doses, it may be due to an additive effect of methanol.

The present study results were compared with the present available literature that shows variation in antimicrobial property of antidiabetic drug metformin that may be due to the solvent that had been used and the concentration of metformin.

SUMMARY & CONCLUSION

Present study results indicate that metformin is active against P. aeruginosa and not active against E.coli. A group of organisms need to be tested to decide the use of metformin as an antimicrobial agent. Metformin antimicrobial action might be beneficial for diabetic patient along with its antihyperglycemic action because the diabetic patients are more prone to develop infections. Metformin as non-antibiotic antibacterial drug may reduce the morbidity in diabetic patients.

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