

***In-vitro* study of Antibacterial Activity of cardiovascular drug Dobutamine hydrochloride**

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Abstract:

In-vitro screening of the cardiovascular drug Dobutamine hydrochloride is conducted in the present research with respect to Gram-negative and Gram positive bacterial strains isolated from blood samples obtained from pathology labs of Nagpur city. It was noticed that most isolated bacterial strains failed to grow at 50-200 µg/mL concentrations of the drug. Dobutamine hydrochloride found to be effective against bacterial action and proved to be bacteriostatic in nature in vitro conditions against both Gram negative and Gram positive bacteria.

Key words: Dobutamine Hydrochloride, Gram-negative and Gram positive.

Introduction:

Antibiotics are one of the most important weapons in fighting against bacterial infections and have greatly benefited the health related quality of human life since their introduction (Sarkar, A. *et al.*, 2003). The therapeutic efficacies of antibiotics and antibacterial agents to cure almost all major infections are gradually becoming limited due to the ever increasing problem of emergence of drug resistances among bacterial pathogens (Dasgupta, A. and Dastidar, S.G. 2012). It is essential to investigate newer drugs with lesser resistance. Systematic studies among various pharmacological compounds have revealed that any drug may have possibility of possessing diverse functions (Sarkar, A. *et al.*, 2003). During the last three decades a large number of compounds belonging to different pharmacological categories have been found to carry moderate to powerful antimicrobial action (Kristiansen, J.E. 1992);(Molnar, J. *et al.*, 1976). The multifunctional nature of most medicinal agents has proved more to be the rule rather than the exception. Positive results were obtained for many drugs falling almost invariably under one of the following groups, namely psychotropics, neuroleptics, local anaesthetics, anti hypertensives, antihistaminics, cardiovascular and antiinflammatory agents (Dasgupta, A. *et al.*, 2007). Drugs belonging to different pharmacological classes such as antihistamines (Dastidar, S.G. *et al.*, 1976), anti hypersensitives (Dastidar,S.G. *et al.*, 1986), local anaesthetics (Dastidar, S. G *et al.*, 1988) and anti-inflammatory drugs (Annadurai, S. *et al.*, 1998) possess powerful antibacterial activity. In the present investigation, a cardiovascular drug named as Dobutamine hydrochloride is used to screen its antibacterial activity. It is essentially a heart stimulating drug with many similarities to dopamine. It has comparable structure but ends at the amine group are not substituted. It has an extra ring which means it is too bulky to activate dopamine receptors and cause norepinephrine release. It is used in intelligent chemically interfective cardiovascular processes.

Material and methods:

Drug: The cardiovascular drug Dobutamine Hydrochloride was obtained in pure dry powder form from Sun Pharmaceuticals, India and was preserved at 4°C.

Bacteria: The bacteria used in the experiment were isolated from blood samples collected from pathology laboratories at Nagpur city. In total 18 isolates were obtained, out of which only four strains(S1A,S1B,S2,S3) were selected and biochemically tested as given in table no.1.They were then followed up to screen antibacterial activity of Dobutamine hydrochloride. These were clinical isolates, identified by as described by Barrow and Feltham in 1993.

S1A- Escherichia coli S1B-Kleibsellla S2-Proteus S3-Pseudomonas.



Media: The media used in this experiment is both liquid and solid media.

Liquid Media used was Nutrient broth (NB:Oxoid). Solid media used was Nutrient agar(, Muller Hinton agar(MHA:Difco), obtained by solidifying liquid media with 1.2%(w/v) agar. The pH of the media was maintained at 7.2-7.4 for all media (Sarkar, A. *et al.*, 2003).

Determination of minimum inhibitory concentration (MIC) of Dobutamine hydrochloride. During the present investigation, MIC was performed by both by agar and broth dilution methods. Dobutamine hydrochloride was added at concentrations of 0 (control), 10, 25, 50, 100 and 200 µg/mL in molten NA and poured into Petri-dish according to NCCLS, 1993. The organisms were grown in NB for 18 h and harvested during the stationary growth phase. A direct suspension of the organisms was prepared in 5 mL sterile distilled water and inoculated onto the NA plates containing increasing amounts of the drug, including a control. The plates were incubated at 37⁰C, examined after 24 h and incubated further for 72 h, whatever necessary. The lowest concentration of the drug in a plate that failed to show any visible macroscopic growth was considered as its MIC. The MIC (MIC 50 and MIC 90) determination was performed in triplicate for each organism and the experiment was repeated where necessary (Dasgupta, A. *et al.*, 2007).

Result and discussion:

Among 18 isolates, only bacterial strains were screened against antibacterial activity of cardiovascular drug Dobutamine hydrochloride. These isolate were all gram negative as biochemically tested mentioned in Table no.1. The MIC was determined by adding organism onto NA plates with increasing amounts of drug as shown in Table no.2. The MIC was determined by both broth dilution and agar dilution method as given in Table no.2 and 3. It was noticed that most isolated bacterial strains failed to grow at 50-200 µg/mL concentrations of the drug. Dobutamine hydrochloride found to be effective against bacterial action and proved to be bacteriostatic in nature *in vitro* conditions against both Gram negative and Gram positive bacteria as shown by Dasgupta, A. *et al.*, 2007 who used The cardiovascular drug lacidipine to screen *in-vitro* for possible antibacterial activity with respect to 389 Gram positive and Gram-negative bacterial strains. It was noticed that most bacteria (233) failed to grow at 50-200 µg/mL concentrations of the drug. Some strains were inhibited at even lower concentrations.

Dobutamine was seen to possess powerful inhibitory action (5-200mg/ml) against test most test bacteria in *in-vitro* studies (Sarkar, A. *et al.*, 2003)

Muzumdar, K., *et al.*, 2003 also performed the experiment with ten cardiovascular drugs, having diverse pharmacological action and were screened for possible antimicrobial property against known eight sensitive bacteria, belonging to Gram positive and Gram negative types. Although five drugs failed to show antimicrobial activity and three had moderate antimicrobial action, oxyfedrineHCl and dobutamine were seen to possess pronounced antimicrobial property.

The present study indicates the potential of Dobutamine hydrochloride as a noteworthy antimicrobial agent, because such properties are likely to improve its usage in humans. The antimicrobial efficiency of Dobutamine can be increased by structural modifications or by combining Dobutamine with conventional antimicrobial agents to produce synergism.

Table no.1: Biochemical test of clinical isolates

Test Sample	Glu	Suc	Mann	Indole	MR	VP	Cit	TSI Acid gas	Gram staining	Shape	Motility
S1A	A	-	A	+	+	+	-	+	Gram negative	Cocco bacilli	Sluggish motile
S1B	AG	AG	AG	-	-	+	+	+	Gram	Long	Motile



									negative	rods	
S2	-	-	-	+	+	-	-	+	Garm negative	Rods	Actively motile
S3	-	-	-	-	-	-	-	+	Garm negative	Rods	Actively motile

S1A-E.coli S1B-Klebsiella S3-Proteus S4-Pseudomonas

Table no.2: Broth dilution method

Dobutamine HCL($\mu\text{g/ml}$) Sample	Control	2	5	10	25	50	100	200	MIC (μl)
S1A	+	+	+	+	+	-	-	-	50
S1B	+	+	+	+	+	+	-	-	100
S2	+	+	+	+	+	+	-	-	100
S3	+	+	+	+	+	-	-	-	50

Table no.3: Agar dilution method

Dobutamine HCL($\mu\text{g/ml}$) Sample	Control	2	5	10	25	50	100	200	MIC (μl)
S1A	+	+	+	+	+	+	-	-	100
S1B	+	+	+	+	+	-	-	-	50
S2	+	+	+	+	+	-	-	-	50
S3	+	+	+	+	+	+	-	-	100

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