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Potential of Dopamine Hydrochloride as a Novel Antimicrobial Agent

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ABSTRACT

The sympathomimetic drug dopamine HCl (HCl) showed significant *in vitro* antibacterial activity against 389 strains of bacteria belonging to 3 Gram-positive and 11 Gram-negative genera. The minimum inhibitory concentration (MIC) of the drug, as determined both by agar dilution and broth dilution methods ranged from 25-400 µg/ml against most bacteria tested, including several pathogenic ones, in the *in vitro* studies. Dopamine HCl was bacteriostatic in action. In an *in vitro* study for combination effect of dopamine HCl with other antimicrobial drugs, this agent showed significant synergistic activity against five different Gram-positive and -negative bacterial strains. Dopamine HCl acts synergistically with antibiotics like penicillin, streptomycin, chloramphenicol, erythromycin, triflupromazine and methdilazine when tested *in vitro* against Gram-positive and Gram-negative bacteria like *Staphylococcus aureus*, *Vibrio cholera*, *Salmonella typhimurium* and *Shigella boydii. In vivo* studies with this drug showed that it could offer statistically significant protection ($P < 0.001$) to mice challenged with a virulent bacterium. Thus dopamine HCl has immense potential to be developed as an antibacterial agent.

Keywords: antibacterial activity, bacteriostatic, non-antibiotic, sympathomimetic, synergistic

INTRODUCTION

The discovery of antibiotics and antibacterial chemotherapeutics acted like a magic bullet against microbial infections at first. However, the massive use of antibiotics, quite often indiscriminately, had caused the earlier euphoria to evaporate, replacing it with the occurrence of drug-resistant bacteria. Studies in this line have disclosed notable antimicrobial action in drugs belonging to different pharmacological classes such as antihistamines like bromodiphenhydramine and diphenhydramine (Dastidar *et al*. 1976), methdilazine (Chattopadhyay *et al*. 1998), promethazine (Chakrabarty *et al*. 1989), trimeprazine (Dastidar *et al*. 1997); tranquillizers like promazine (Chakraborty *et al*. 1977); antihypertensives like propranolol (Manna *et al*. 1984), methyl DOPA (Dastidar *et al*. 1986), dobutamine (Sarkar *et al*. 2003), amlodipine (Kumar *et al*. 2003; Dutta *et al*. 2009), nifedipine (Pal *et al*. 2006), oxyphedrine (Mazumdar *et al*. 2003); antispasmodics like dicyclomine (Karak *et al*. 2003, 2004); antipsychotics like chlorpromazine (Amaral *et al*. 1991), fluphenazine (Dastidar *et al*. 1995), thioridazine (Radhakrishnan *et al*. 1999); the anti-inflammatory agent diclofenac (Annadurai *et al*. 1998, 2002; Dastidar *et al*. 2002, 2003; Dutta *et al*. 2007). Such drugs, having antimicrobial activity in addition to their predesignated pharmacological action, have been grouped together under the banner of "non-antibiotics" (Kristiansen 1992). The present study describes the detailed *in vitro* and *in vivo* antimicrobial activity of such a non-antibiotic: the sympathomimetic drug dopamine hydrochloride (HCl) and thereby assisting the search for newer types of antimicrobial agents for solving difficult chemotherapeutic problems.

MATERIALS AND METHODS

Drug

Dopamine is a natural precursor of nor-adrenaline and adrenaline. It is also a neurotransmitter of the central and peripheral nervous system. Dopamine HCl (**Fig. 1**) is a white crystalline powder having a molecular weight of 189. Chemically it is 1,2-benzenediol,4-(2-aminoethyl) HCl or 3,4-dihydroxy phenethylamine HCl, decomposes at about 241°C, is freely soluble in water, soluble in alcohol, and practically insoluble in chloroform or ether (Remington 1995).

Dopamine HCl was obtained as a gift from Vulcan Laboratories Pvt. Ltd., Kolkata in pure dry powder form and was kept at 4°C, being protected from light.

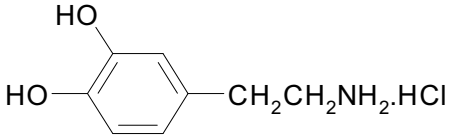

Fig. 1 Structure of dopamine HCl.

Bacteria

A total of 389 bacteria belonging to 3 Gram-positive and 11 Gram-negative genera and comprising of 115 Gram-positive and 274 Gram-negative strains were tested (**Table 1, Fig. 2**). Many of these were of human origin, identified as described by Barrow and Feltham (1993) and preserved in a freeze-dried state.

Media

Liquid media used for this study were peptone water [PW; Oxoid brand bacteriological peptone 1% (w/v) plus Analar NaCl 0.5% (w/v)], nutrient broth (NB; Oxoid), Muller-Hinton broth (MHB;

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Table 1 *In vitro* activity of dopamine on Gram-positive and Gram-negative bacteria.

Bacteria	№ tested	№ of strains inhibited by dopamine hydrochloride (µg/ml)						
		10	**25**	**50**	**100**	**200**	**400**	**>400**
Staphylocccus aureus	103	15	16	21	32	13	-	6
Bacillus spp.	10	-	-	1	5	1	-	3
Streptococcus spp.	2	-	-	-	-	2	-	-
Escherichia coli	50	4	2	1	9	8	3	23
Klebsiella spp.	6	-	-	-	1	2	3	-
Salmonella spp.	19	-	1	5	2	3	2	6
Shigella spp.	48	1	3	4	8	16	8	8
Hafnia spp.	1	-	-	1	-	-	-	-
Proteus spp.	7	-	-	-	-	-	-	7
Providencia spp.	1	-	-	-	-	-	-	1
Arizona spp.	1	-	-	-	-	-	-	1
Bordetella bronchiseptica	1	-	-	-	-	1	-	-
Vibrio cholerae	102	3	19	28	21	12	8	11
Vibrio parahaemolyticus	30	5	11	7	7	-	-	-
Pseudomonas spp.	8	-	-	-	-	2	1	5
Total	389	28	52	68	85	60	25	71

Difco). Solid media were desoxycholate citrate agar (DCA, Oxoid) and peptone agar (PA), nutrient agar (NA) and Muller-Hinton agar (MHA), obtained by solidifying the liquid media with 1.2% (w/v) agar (Oxoid No. 3). The pH was maintained at 7.2-7.4 for all media. NA was used for Gram-positive bacteria while PA and DCA were used for the rest of the bacteria.

Determination of minimum inhibitory concentration (MIC) of dopamine

The MIC of the drug with respect to different test bacteria was accurately determined both by broth and agar dilution methods. For broth dilution (NCCLS 1993) 0.1 ml of standardized suspension of a strain [10^5 Colony Forming Units (CFU)/ml] was added to each tube containing a drug at concentrations of 0 (control), 10, 25, 50, 100, 200 and 400 µg/ml in MHB. The tubes were incubated at 37°C for 24 h and observed for visible growth after vortexing the tubes gently. For agar dilution, the drugs were added at concentrations of 0 (control), 10, 25, 50, 100, 200 and 400 µg/ml in molten NA and poured into Petri dishes (Koneman 1997). The organisms were grown in PW, and the overnight culture was spot inoculated on the NA plates such that each inoculum contained 2×10^5 CFU. The plates were incubated at 37°C, examined after 24 h and incubated for further 72 h, if there is no significant growth to naked eye after 24 h. Since one NA medium containing a drug can be used for inoculation of a large number of bacteria at a time, the result of this method is presented in **Table 1**, as the total number of tested bacteria is 389. The lowest concentration of a drug in a tube or plate that failed to show any visible macroscopic growth was considered as its MIC. The MIC determination was performed in duplicate for each organism; the experiment was repeated where necessary to have identical results in a duplicate set of experiments. The MIC values for a given isolate were either identical or within ± one dilution.

Determination of synergism, antagonism and indifference in the assay of dopamine with different antibiotics and non-antibiotics

The combined effect of two agents *in vitro* was performed by the disc diffusion technique as described by Miles and Amyes (1996). The discs were placed at suitable (average diameter of zone of inhibition of individual drugs) distances apart so that the respective agents would not diffuse into one another to produce a continuous range of concentrations in the initial period of inhibition. This was done by initial disc sensitivity test of a microorganism with respect to a particular concentration of an agent and determining the diameters of the zone of inhibition; thereafter, the discs of the two agents, whose relationship was to be determined were placed in such a manner that the inhibitory circles would touch each other tangentially, leaving only a very thin ridge of growth, in case of complete indifference. In the case of antagonism, the circles would recede away from each other at their facing surface assuming a somewhat kidney shape; while in case of synergism, the ridge of growth would disappear and the two circles would merge to form a single asymmetric ellipse (Garrod *et al*. 1981).

Determination of the mechanism of action of dopamine HCl on *V. cholerae* ATCC 14033 and *S. aureus* NCTC 8531

To determine the mode of action of dopamine HCl on different bacterial strains one member from the Gram-positive (*S. aureus* NCTC 8531) and one member from the Gram-negative (*V. cholera* ATCC 14033) genera were chosen as a representative since the behavioral pattern of other members of the genera are expected to be similar. *V. cholerae* ATCC 14033 and *S. aureus* NCTC 8531 were individually grown in NB overnight at 37°C. From each such culture 2 ml was added to 4 ml of fresh NB and incubated at 37°C for 2 h so that the culture could attain the logarithmic growth phase. The number of viable cells was then determined and dopamine HCl was added at a concentration higher than its MIC value with respect to *V. cholerae* ATCC 14033 (MIC 25 µg/ml) and *S. aureus* NCTC 8531 (MIC 10 µg/ml). The CFU counts were determined up to 6 h at an interval of 2 h and then after 18 h (Krogstad and Moellering 2005).

In vivo antibacterial activity of dopamine HCl

The Swiss strain of male white mice weighing 18-22 g was used for the *in vivo* studies. Animals were maintained at standard conditions at 21 ± 1°C and 50-60% relative humidity with a 14-h photoperiod. Water and a dry pellet diet were given *ad libitum*. The virulence of the test strain *S. typhimurium* NCTC 74 was exalted by repeated mouse passages and the median lethal dose (MLD or LD_{50}) of the passaged strain was determined. From this the 50×MLD of the strain corresponding to 0.95×10^9 CFUs/mouse suspended in 0.5 ml NB served as the challenge dose (Dutta *et al.* 2009) for all groups of animals. Reproducibility of the challenge dose was ensured by standardization of its optical density in a Klett-Summerson colorimeter at 640 nm and determination of the CFU count in NA (Miles and Misra 1938).

To determine the toxicity of dopamine HCl, 40 mice were taken, 20 of which were injected with 60 µg of the drug, while the remaining 20 received 30 µg of dopamine HCl. They were kept under observation for up to 100 h.

The protective capacity of dopamine HCl was judged as follows: two groups of mice, 20 animals per group, were kept in separate cages. Group I was intraperitonially (i.p.) administered 30 µg dopamine HCl/mouse, and group II was given 60 µg of the drug/mouse. After 3 h, each group was challenged with 50 MLD of *S. typhimurium* NCTC 74. A control group of 40 mice was also injected similarly with the same bacterial strain and 0.1 ml sterile saline instead of dopamine. The protective capacity of the drug was determined by recording the mortality of mice in different groups up to 100 h of treatment, and statistically by the χ^2 test.

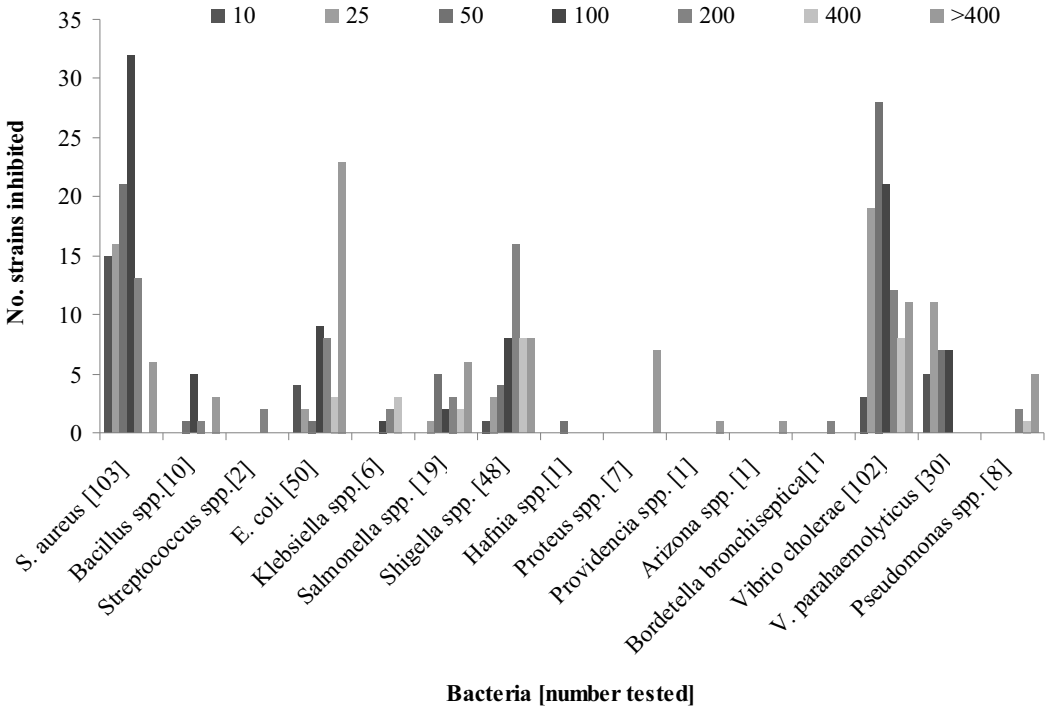

Fig. 2 Antibacterial spectrum of dopamine HCl.

In another experiment, 4 groups of mice, 5 animals per group, were used. Group 1 and 3 were administered intraperitonially 60 µg of dopamine, while group 2 and 4 were given 0.1 ml sterile saline. After 3 h, all groups were given a 50 MLD challenge of *S. typhimurium* NCTC 74. After 2 h, groups 1 and 2 were sacrificed. Their heart blood was collected aseptically; their livers and spleens were removed aseptically and homogenized in tissue homogenizers. CFU count of the individual organs was determined separately. The same procedure was applied to groups 3 and 4, 18 h after challenge; statistical analysis of the *in vivo* data was carried out by the Student's *t*-test at $P < 0.05$. All the animal experiments were performed following institutional animal ethics committee guidelines of Gupta College of Technological Sciences, Asansol (955/A/06/CPCSEA 2006).

RESULTS

In vitro antimicrobial action of dopamine HCl

A preliminary screening of dopamine HCl against 11 known sensitive bacteria belonging to both Gram-positive and Gram-negative genera showed a powerful antimicrobial action against most of the test bacteria.

In an elaborate *in vitro* study (**Table 1, Fig. 2**), the drug was tested against 389 strains of bacteria belonging to 3 Gram-positive and 11 Gram-negative genera. Most of these were inhibited by the drug at the 10-100 µg/ml level and a few were sensitive even at lower concentrations. The descending order of sensitivity of bacteria towards dopamine was: *S. aureus*, *V. parahaemolyticus*, *V. cholerae*, *Shigella* spp., *Salmonella* spp., and *Bacillus* spp., whereas a few strains of *E. coli*, *Klebsiella* and *Pseudomonas* spp. were inhibited at much higher concentrations (400-600 µg/ml) of the drug.

In vitro study on the effect of combination of dopamine with other antimicrobial drugs for synergism, antagonism and indifference

In the *in vitro* study of synergism, antagonism or indifference of the combination of effects between dopamine HCl and other non-antibiotics were determined by the disc diffusion technique. The amount of dopamine HCl/disc was 400 µg and that of an antibiotic was 5 µg/disc, the dose being chosen to be the MIC values of dopamine HCl and that of antibiotic. The drug-impregnated discs were prepared in screw-capped bottles and stored at 4°C as described by Cruickshank *et al.* (1975). The medium for the disc diffusion test was basically NA for Gram-positive bacteria and PA for Gram-negative bacteria. The Gram-positive bacterial strains tested were *S. aureus* NCTC8530, *S. aureus* NCTC8531 and among the Gram-negative strains *V. cholerae* ATCC14033, *S. typhimurium* NCTC74 and *Sh. boydii* 8 NCTC 254/66.

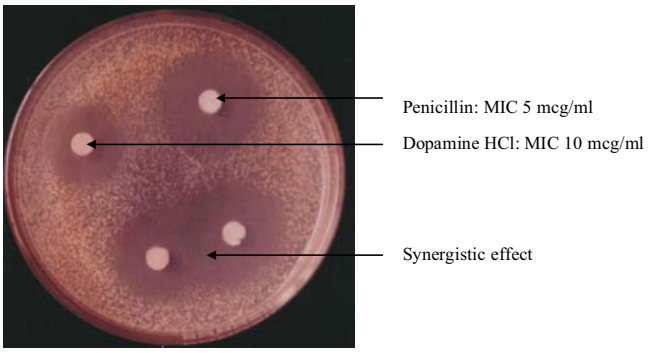

Fig. 3 Synergism of dopamine with penicillin on *S. aureus* NCTC8530. Zone of Inhibition of penicillin and dopamine HCl on *S. aureus* NCTC 8530 is 18 mm and 10 mm, respectively individually and 25 mm and 15 mm in combination proves synergism.

The drug dopamine HCl showed synergistic effects with penicillin (Pc) (**Fig. 3**), streptomycin (Sm), chloramphenicol (Cm), erythromycin (Em), triflupromazine (Tf) and methdilazine (Md); It also produced an antagonistic effect with gentamicin (Gm) but was indifferent to tetracycline (Tc) and diclofenac sodium (Dc) (**Tables 4, 5**). Synergism of dopamine HCl with penicillin on *S. aureus* NCTC 8530 was demonstrated (**Fig. 3**).

Protective capacity of dopamine HCl *in vivo*

Table 2 shows that in the control group, 49 out of 60 animals died within 100 h of the challenge and no mortality was recorded in those groups of mice that received different

Table 2 Determination of *in vivo* protection by dopamine HCl.

Control group*		Test group*	
Drug injected per mouse	Mice died (out of 60)	Drug injected per mouse	Mice died (out of 20)
0.1 ml sterile saline	49	30 µg	13
		60 µg	4

*Received a challenge dose of 0.95×10^9 cfu in 0.5 ml NB of *S. typhimurium* NCTC 74. None of the animals died when 30 or 60 µg dopamine was injected to 2 separate groups of mice (20 mice in each group), i.e., dopamine was found to be non-toxic to mice. $P < 0.001$, according to χ^2 test.

doses of dopamine HCl only. There was significant protection ($P < 0.001$) in the drug-treated groups by dopamine HCl.

In **Table 3** and **Fig. 4**, it may be seen that dopamine HCl significantly reduced the number of viable bacteria in heart blood, liver and spleen of mice, both at 2 and 18 h after challenge, compared with the control (saline-treated) mice. Statistical analysis showed $P < 0.05$ for 2-h samples and $P < 0.01$ for 18-h samples. Viable counts between two groups were significant; $P < 0.05$ in 2-h samples and $P < 0.01$ in 18-h samples.

Determination of mode of action of Dopamine HCl

The MIC of dopamine HCl against *V. cholerae* ATCC 14033 was 25 µg/ml and on *S. aureus* NCTC 8531 was 10 µg/ml; in the logarithmic growth phase, their CFU counts were 12×10^8 and 6.3×10^8, respectively. At the 0 (zero) hour, 2 × MIC of dopamine for the test organisms was added to each of the culture tubes. Subsequently, when the CFU counts were determined after 2, 4, 6 and 18 h, it was noticed that there was a gradual decrease in the number of viable cells up to 4 h for both bacteria. However, there was no further decrease in the number of viable cells, proving the bacteriostatic property of the drug.

DISCUSSION

Pharmaceutical industries and research organizations are constantly making an effort to synthesize new antibiotics to combat drug resistance. The search for antimicrobials has now been extended to a class of compounds named "non-antibiotics" which are employed for the therapy of non-infectious pathologies and which demonstrate significant antimicrobial activity against some of the most pathogenic infectious agents such as vancomycin-resistant or methicillin-resistant *S. aureus* (Martins *et al*. 2004), or multi-drug resistant *Mycobacterium tuberculosis* (Ordway *et al.* 2003; Amaral *et al.* 2007; Martins *et al.* 2008).

Dopamine HCl, being a sympathomimetic drug, is used in conditions of low cardiac output with compromised renal function, such as cardiogenic and hypovolemic shock (Seth 1998). In the treatment of congestive cardiac failure refractory to other drugs dopamine HCl can be used. It is also given to patients of pheochromocytoma after surgical removal of the tumor. Dopamine, when given parenterally, does

Table 3 Efficacy of dopamine HCl in reducing bacterial counts in challenged mice.

Time in hours	Group	No of mice	Drug/ Mouse	CFU/ml counts in		
				Heart blood	Liver	Spleen
2	I	5	Dopamine HCl (60 µg)	2.1×10^3, 2.3×10^3, 2.5×10^3, 3.1×10^4, 5.6×10^3	1.1×10^3, 3.0×10^3, 6.5×10^4, 2.1×10^3, 1.2×10^4	4.3×10^3, 4.6×10^3, 1.2×10^3, 6.2×10^3, 2.5×10^4
2	II	5	Saline (control)	4.0×10^5, 5.5×10^4, 6.5×10^4, 6.0×10^4, 7.8×10^6	2.8×10^6, 4.6×10^6, 6.5×10^6, 7×10^6, 8.5×10^6	1.2×10^5, 8.4×10^6, 5.4×10^6, 8.6×10^5, 8.8×10^6
18	III	5	Dopamine HCl (60 µg)	1.1×10^3, 2.6×10^3, 3.6×10^4, 4.5×10^4, 7×10^3	5.8×10^3, 7.3×10^4, 3.8×10^4, 2.3×10^4, 7.1×10^4	7.8×10^5, 3.5×10^3, 7.2×10^3, 4.0×10^4, 3.4×10^4
18	IV	5	Saline (control)	5.4×10^8, 4.7×10^9, 6.8×10^8, 5.6×10^9, 7.2×10^9	5.8×10^8, 2.7×10^9, 3.9×10^4, 8.0×10^8, 5.2×10^9	1.8×10^8, 5×10^8, 5.4×10^9, 4.9×10^8, 8.2×10^9

Table 4 *In vitro* combination effect of dopamine HCl with other antimicrobial drugs.

Organisms		Zone of inhibition (mm) for different combination of drug (µg/disc)				
		Pc (5), Dp (400)	Sm (5), Dp (400)	Gm (5), Dp (400)	Cm (5), Dp (400)	Tc (5), Dp (400)
S. aureus NCTC8530	Individual	18, 10	18.5, 16.5	20, 12	19.5, 16	18.5, 15
	Combined	25, 15	22.5, 19.5	15, 10	23.5, 19	18.5, 15
S. aureus NCTC8531	Individual	18, 10	18, 16	19.5, 12	19.5, 16	17.5, 14.5
	Combined	26, 15	22.5, 19	15.5, 10	23.5, 19	17.5, 14.5
V. cholerae ATCC14033	Individual	20, 15	20, 17	22, 14	20, 15.5	24, 18
	Combined	21, 16	22.5, 18.5	20, 12	25, 19	24, 18.5
S. typhimurium NCTC 74	Individual	15, 14	17.5, 15	24, 14	18, 15.5	21, 15.5
	Combined	16, 16	18.5, 16	20, 10	19.5, 16.5	21, 15.5
Sh. boydii 8 NCTC 254/66	Individual	16.5, 15.5	15, 15	24.5, 12.5	20.5, 15.5	22, 15
	Combined	18.5, 16.5	17, 15.5	22.5, 10.5	24.5, 19	22, 15
Conclusion		Synergism	Synergism	Antagonism	Synergism	Indifference

Dp: Dopamine HCl; Pc: Penicillin; Sm: Streptomycin; Gm: Gentamicin; Cm: Chloramphenicol; Tc: Tetracycline

Table 5 *In vitro* combination effect of dopamine HCl with other antimicrobial drugs.

Organisms		Zone of inhibition (mm) for different combination of drug (µg/disc)			
		Em (5), Dp (400)	Tf (200), Dp (400)	Dc (200), Dp (400)	Md (150), Dp (400)
S. aureus NCTC8530	Individual	19, 15	16.5, 15	18, 15	14, 15
	Combined	26, 20	17.5, 15.5	19, 15.5	18, 20
S. aureus NCTC8531	Individual	19.5, 15	15, 14.5	18.5, 15	14.5, 16
	Combined	26, 20	18, 16	19, 15	19.5, 21
V. cholerae ATCC14033	Individual	20, 15.5	13.5, 13	17, 14	13, 15.5
	Combined	24.5, 19.5	18, 18	17.5, 14.5	14, 15.5
S. typhimurium NCTC 74	Individual	20.5, 17	13.5, 14.5	18.5, 16	14.5, 15
	Combined	24, 20	18.5, 18.5	18.5, 16.5	15.5, 16
Sh. Boydii 8 NCTC 254/66	Individual	21, 16.5	12, 14	17, 15	16, 17
	Combined	25, 18.5	17.5, 17	17, 15.5	16.5, 17
Conclusion		Synergism	Synergism	Indifference	Synergism

Dp: Dopamine HCl; Em: Erythromycin; Tf: Triflupromazine; Dc: Dicolfenac sodium; Md: Methdilazine

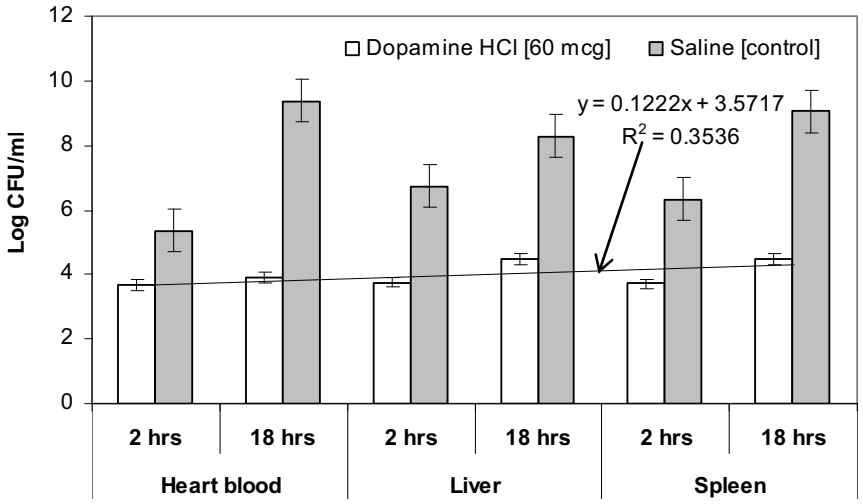

Fig. 4 Efficacy of dopamine HCl in reducing CFU in challenged mice.

not cross the blood-brain-barrier and hence has no central effect. It is orally ineffective, destroyed in the body by both MAO and COMT, and has a very short duration of action. Its main action is on the cardiovascular system. When it is given intravenously in a small dose, it acts on the D_1 receptor and causes selective dilatation of renal vessels, resulting in increased glomerular filtration rate, renal blood flow and excretion of sodium. In a higher concentration (over 10 to 12 µg/kg/min), it stimulates the β_1 receptor and causes increased force of contraction of myocardium with less tachycardia (Remington 1995).

Dopamine HCl is dissolved in 5% glucose solution to a concentration of 0.4 to 1.6 mg/ml. It is given by slow intravenous infusion at a rate of 2-5 µg/kg/min and gradually increased to 20 µg/kg/min under constant monitoring of blood pressure, urinary output, heart rate and arrhythmias. The half-life is only 2 min and therefore it should be tapered off slowly (Seth 1998). During infusion, patients require clinical assessment of myocardial function, perfusion of vital organs such as the brain, and the production of urine (Goodman and Gillman 2005).

In addition to these pharmacological actions, dopamine HCl has significantly inhibited several Gram-positive and -negative bacteria *in vitro* and *S. typhimurium in vivo*. The antibacterial activity of the drug was noteworthy with respect to different strains of *Staphylococcus*, *Vibrio*, *Shigella*, *Salmonella*, *E. coli* and *Bacillus* whereas a few strains of these bacteria were inhibited at higher concentrations of dopamine (**Table 1**).

While deciding a suitable therapy for a particular microbial infection, the foremost criterion that a clinician takes into account is the MIC of an antimicrobial agent. In many cases, two drugs have been simultaneously used against a microbe, after obtaining the susceptibility profiles of the agents. However, due to the escalating frequency of multidrug resistant organisms, very often only one agent (or one class of agents) remains to which the pathogen is susceptible. In such cases, monotherapy may be preferred, but such treatment might be sub-optimal, if not a failure altogether. Therefore, it is obvious that the advantage of combination therapy (preferably synergism) is obtained only when the concerned organism is susceptible to both agents (Mazumdar *et al.* 2005).

In the present study, enhancement of antimicrobial activity of some common antibiotics was achieved when used in combination with dopamine HCl. In the *in vitro* study on the effect of combination of dopamine HCl with other antimicrobial drugs dopamine showed synergistic effects with penicillin, streptomycin, chloramphenicol, erythromycin, triflupromazine and methdilazine. The drug produced an antagonistic effect with gentamicin indicating its incompatibility, while tetracycline and diclofenac sodium were

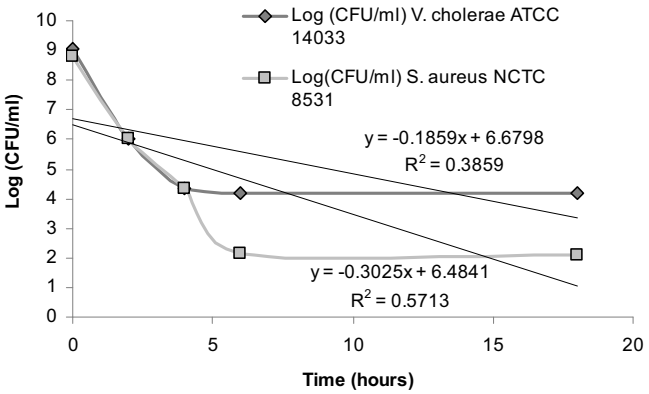

Fig. 5 The mode of action of dopamine on *V. cholera* ATCC14033 and *S. aureus* NCTC 8531.

indifferent with dopamine HCl (**Tables 4, 5**).

Dopamine was non-toxic to mice. *In vivo* studies using Swiss albino male mice and *S. typhimurium* NCTC 74 were statistically significant (**Tables 2, 3**). The mode of action of dopamine on Gram-positive and -negative bacteria was bacteriostatic (**Fig. 5**).

Examination among various classes of pharmacological agents has revealed that in general, the tricyclic phenothiazines possess a discernable antimicrobial action (Bourlioux 1992). Extensive reviews of the literature have revealed that antimicrobial properties of several phenothiazines and other antimicrobial agents are due to the presence of aromatic rings (Kristiansen *et al.* 1997; Dasgupta *et al.* 2007, 2008). A search for antimicrobial action among antihypertensives led to the discovery of yet another compound, methyl-DOPA (Dastidar *et al.* 1986). This compound possesses only one benzene ring and therefore just one benzene ring could be responsible for such activity. Dopamine HCl is already in standard use, convincing therapeutic requirements, and it is in compliance with human toxicity levels (Michel *et al.* 1990). Thus, this drug stands a chance of being developed as an antimicrobial agent alone and in combination with other antimicrobial agents against common bacterial infections with a view to designing a new generation of promising non-antibiotic drugs to combat bacterial drug resistance.

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