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Synergistic Effects of Traditional and Conventional Medicines

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Abstract
In our daily life we encounter a lot many organisms. Many of them are so small that they can't be seen with the naked eyes. We might as well not feel their presence. Our body's immune system is so very capable of resisting any changes induced by them or by their presence but it should also be known that some of these organisms have developed methods or are so capable to resist even our immune system. Hence, they show their superiority over us by inflicting us with disease. We often rely on the medicines that contain various chemical substances to tackle with these diseases. Also these chemicals are not 100% safe to use, meaning; they have certain side effects along with their curing capabilities. These effects might not be seen instantaneously but can be felt in a long term. It has almost been the whole time that the man is searching for these types of products that can cure our illness without leaving any side effect. So the focus is shifted towards the plant products that are known to be comparatively friendly [1, 2]. The medicinal properties of plant products have been known to man for quite a long time and many tribal as well as city population still practice its use. There is now a lot of research going on to find the various plant products that can be used, whether alone or along with some chemical compound/drug synergistically [3, 4, 5].

Keywords: Antimicrobial activities, bacterial isolates and inhibition zones, aqueous garlic extract, garlic & ciprofloxacin synergism, Bacterial resistance

Introduction
It is evident that many products from the plants along with some chemical compounds have an intensified effect on the disease causing microorganisms. This is known as synergism. But this is not true in all the cases. Many a time the plant products and the antimicrobial drug do not work synergistically. In this review we are going to focus on those combinations that work together to create an effect that is more than the effect created by both of them individually. Various microorganisms are tested for their activity towards a number of different antibiotics and their results are noted. Then these microorganisms are tested upon by individual plant products and similarly the results were noted. Finally the various strains of microorganisms are tested by the combined effect of the antibiotic and the plant product and the results are noted. Individual effect of antibiotic and the plant product is also measured by making different concentrations or ratios of them. It is seen that many strains of the microorganisms have developed resistance against various antibiotics and do not show any clear zone on the petri plates [6]. But when the same strains of microorganisms are exposed to the plant products they show less efficient resistance. And when they are exposed to the mixture of both antibiotic and the plant product, they show a much less efficient resistance. Which provide us the basis to say that the plant products are much efficient individually as well as synergistically to deal with many disease causing microorganisms [7]. It is also known that these plant products don't cause harm to the human body and so are being encouraged.

Studies
Study 1 [8]
The study conducted by Ojiezeh, T. I *et al.* on the activities of bitter leaf (*Vernonia amygdalina*) extract and lime (*Citrus aurantifolia*) juice on total of forty-five pure culture isolates, comprising of five strains each of *E. coli, Pseudomonas aeruginosa, Staphylococcus aureus, α-haemolytic streptococcus, β-haemolytic streptococcus*, *Klebsiella spp, Proteus*

mirabilis, Salmonella typhi and *Shigella dysenteriae* provide us the results that favor the capability of the plant products in medicines. Their studies suggest that five organisms i.e *Pseudomonas aeruginosa, E. coli, Staphylococcus aureus, Klebseilla spp*. and *Proteus mirabilis* were susceptible to the bitter leaf and lime juice crude extract and had a mean zone diameter of inhibition ranging from 18mm to 25mm while the strains of *Pseudomonas aeruginosa, E. coli* and *Staphylococcus aureus* were found to be more sensitive to bitter leaf extract than lime juice extract in in-vitro conditions. It was also seen that the bitter leaf had comparatively much better activity than the lime juice and exhibited a comparatively larger zone of inhibition. The neat i.e 100% pure extract of bitter leaf had the highest range of inhibition zone on the following test organisms: *Pseudomonas aeruginosa, Escherichia coli, Staphylococcus aureus, Klebsiella spp* and *Proteus mirabilis* and it was found out to be 17-28mm (table 1) whereas in case of the neat (100%) extract of lime juice, it was true for the following species *Staphylococcus aureus*, *E. coli, Pseudomonas aeruginosa, Klebsiella spp,* and *Proteus mirabilis* which showed the zone of inhibition ranging from 18-23 mm (table 2).

Table 1: Comparative antimicrobial Sensitivity of ethanol extract of bitter leaf

TEST ORGANISMS	SIZE OF INHIBITION ZONE (mm)					
	Neat	½	¼	1/8	1/16	1/32
Pseudomonas aeruginosa	28	24	20	14	8	5
Escherichia coli	26	23	17	8	5	R
Staphylococcus aureus	25	23	18	10	6	R
Klebsiella spp	24	20	17	12	8	5
Proteus mirabilis	20	15	10	6	R	R
α-haemolytic streptococcus	21	16	9	R	R	R
β-haemolytic streptococcus	19	14	6	R	R	R
Salmonella typhi	18	15	10	6	R	R
Shigella dysenteriae	17	12	8	PS	R	R
CONTROL:						
Staphylococcus aureus (NCTC 6571)	26	23	20	14	9	5
E. coli (NCTC 10418)	27	23	18	10	6	R

R- Resistant, PS- Partially Sensitive (<3 mm); Minimum inhibition Concentration (1/16) for all test organisms except haemolytic streptococci that was (1/8)

Table 2: Comparative antimicrobial sensitivity of lime juice extract

TEST ORGANISM	SIZE OF INHIBITION ZONE (mm)					
	Neat	½	¼	1/8	1/16	1/32
Staphlococcus aereus	22	20	10	6	R	R
E. coli	20	17	8	5	R	R
Proteus mirabilis	19	12	6	PS	R	R
Klebsiella spp	19	15	10	6	R	R
Pseudomonas aeruginosa	17	14	10	5	R	R
α-haemolytic streptococcus	8	5	PS	R	R	R
β-haemolytic streptococcus	8	5	PS	R	R	R
Salmonella typhi	12	7	5	R	R	R
Shigella dysenteriae	8	5	PS	R	R	R
CONTROL:						
Staphylococcus aureus (NCTC 6571)	22	18	10	6	R	R
E. coli –(NCTC 10418)	24	20	13	5	R	R

R- Resistant, PS- partial sensitivity (<3 mm) ; Minimum inhibition concentration 1/8 for all test organisms except haemolytic streptococci and Shigella dysenteriae.

Further the various dilutions of the bitter leaf and lime juice extracts wef. ½, 1/4, 1/8, 1/16, 1/32 had the varying effects and lead to different sizes of zone of inhibition and are mentioned in the above tables. With dilution the inhibitory effect of the extracts decreased. But still the inhibitory effect of the bitter leaf extract was more than the lime juice extract. The results were postulated and compared with the control *Staphylococcus aureus* (NCTC 6571) and *E. coli* (NCTC 10418) that showed mean zone of inhibition of 5 – 9 mm at 1/8 dilution. The comparison between the activity of the two plant products is also shown under:

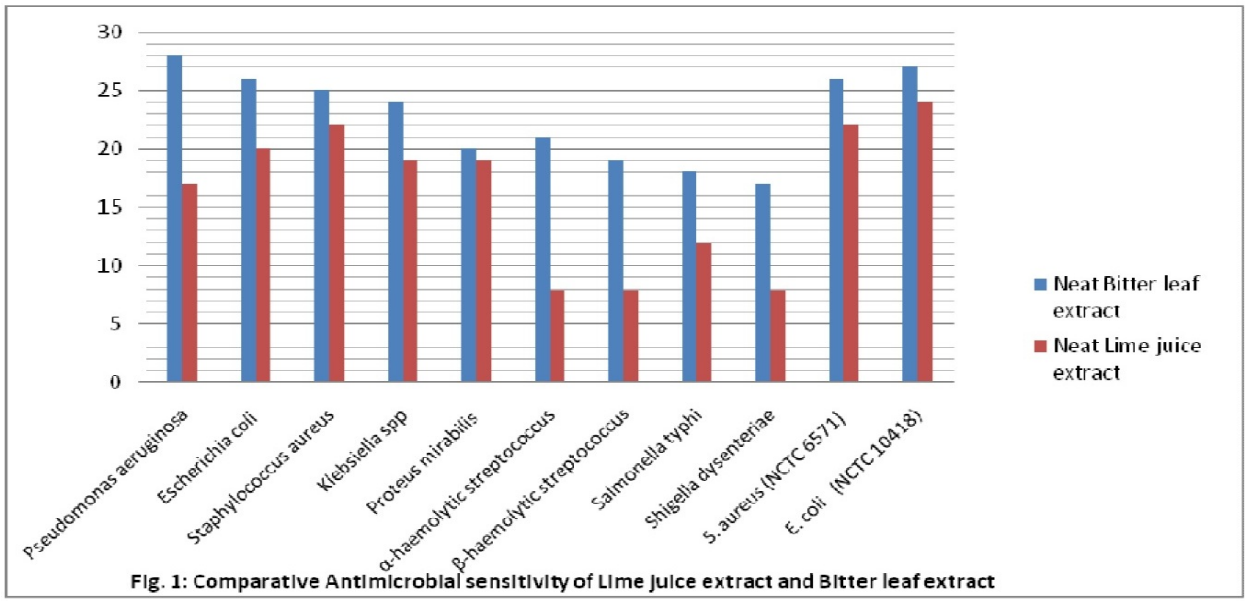

Fig. 1: Comparative Antimicrobial sensitivity of Lime juice extract and Bitter leaf extract

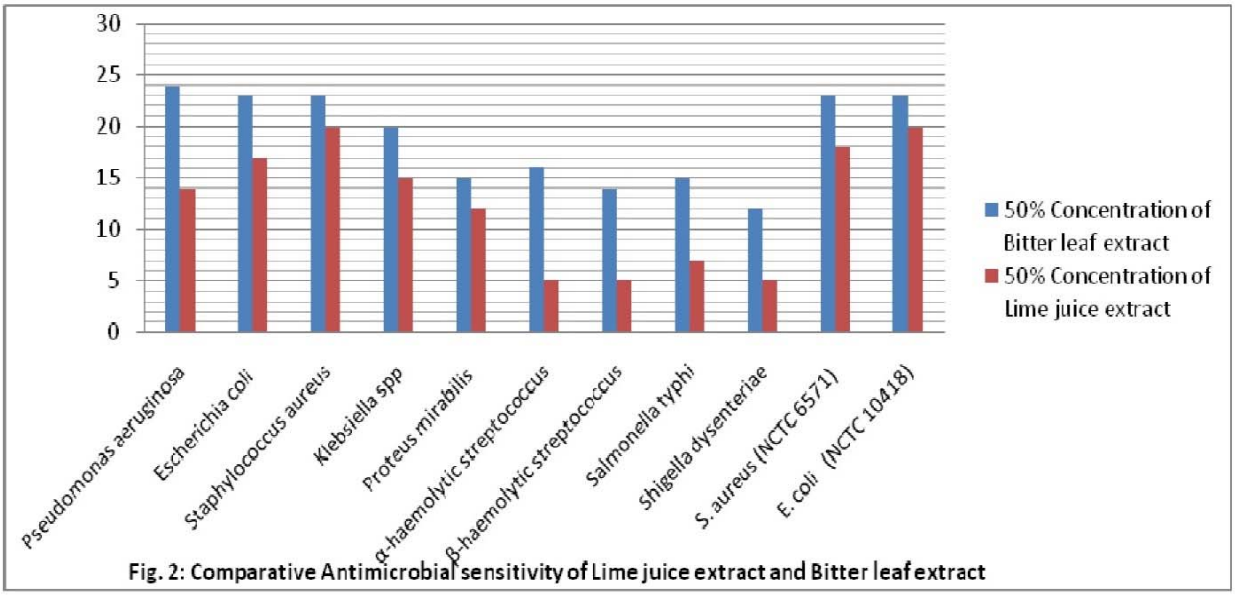

Fig. 2: Comparative Antimicrobial sensitivity of Lime juice extract and Bitter leaf extract

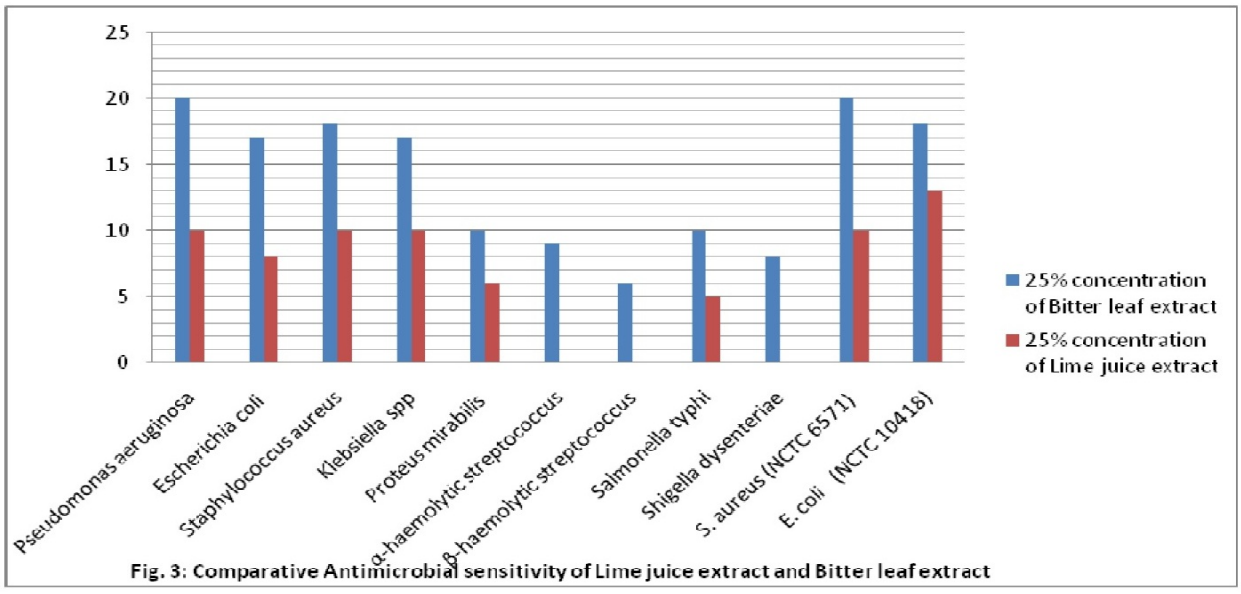

Fig. 3: Comparative Antimicrobial sensitivity of Lime juice extract and Bitter leaf extract

Study-2 [9]

It is evident historically that garlic(Allium sativum) has many therapeutic properties like antimicrobial, antineoplastic, anti-cardio vascular, anti -hypertensive, anti-hyperlipidemia, anti-diabetic, immuno-stimulatory and hypoglycaemic activities [10-15]. In a study related to evaluate the inhibitory effect of aqueous garlic extract(AGE) and its synergism with the two well-known antibiotics i.e ciprofloxacin(CIP) and ampicillin(Am) conducted by Salah Salman Zain al-abdeen, Iman Tajer Abdullah and Sohaib Sabah Al-Salihi of *Department of Biology, Science College, Kirkuk University, Kirkuk, Iraq* against 12 multi-resistant isolates, including two isolates of *Staphylococcus aureus*, three isolates of *Pseudomonas aeruginosa* and seven isolates of *E. coli*, the following are the key features of their study:

A total of 12 strains of microorganisms were selected and are as in the table below

Table 3: Bacterial isolates from pathological samples

Bacteria	Total number	Blood	Urine	Sputum
E.coli	7	1	6	-
Pseudomonas spp.	3	3	-	-
Staphylococcus aureus	2	1	-	1

In their experiments conducted it was found out that the strains they worked on showed multiple resistance patterns and the table below shows the complete results of their experimentation(1)

Table 4: The resistant pattern of isolated bacterial antibiotics

Bacteria	Antibiotics											
	SXT	**DA**	**TE**	**AM**	**CIP**	**E**	**AMC**	**PRL**	**CL**	**TMP**	**PY**	**K**
E.coli 1	23	R	R	R	27	R	R	R	10	20	R	16
E.coli 2	20	R	R	R	35	R	R	R	R	R	R	R
E.coli3	R	R	20	R	26	15	R	R	R	R	R	20
E.coli4	30	30	30	10	30	20	12	10	30	10	30	20
E.coli5	R	R	R	R	20	R	R	R	R	R	R	15
E.coli6	24	R	20	R	30	R	R	R	R	R	R	20
E.coli7	R	R	10	R	35	10	10	27	R	R	R	R
P. aeruginosa 1	R	R	R	R	25	R	R	20	R	R	R	R
P. aeruginosa 2	R	R	R	R	40	R	R	20	R	R	R	R
P. aeruginosa 3	R	R	10	R	30	R	R	23	R	R	R	R
S.aureus 1	25	30	10	R	30	28	15	15	R	30	R	19
S.aureus 2	20	30	30	R	30	24	15	20	30	R	R	R

R:ResistantSXT:Trimethoprime+SulfanamideDA:ClindamycinTE:TetracyclinAM:AmpicillinCIP:Ciprofloxacin E:Erythromycin AMC:Amoxicillin+Clavulanic acid PRL:PipracillinCL: Cephalexin

From the table we can see that antibiotic CIP showed its effect against all the test organisms and for all the strains of *E.coli* the inhibition zone ranged between 20-40 mm. CIP and DA gave the highest inhibition zone which reached 30mm for two isolates and TMP antibiotic used for isolates No. 1 and antibiotics TE and CL for isolate No. 2 while the antibiotic TE gave the smallest inhibition zone for sample against sample no.1 which ranged to 10mm.

Also all the strains of *P. aeruginosa* showed multiple resistance to all the antibiotics except CIP and PRL. CIP gave the highest zone of inhibition i.e 40mm for isolate no. 2 and least inhibition zone was given by TE which was recorded as 10 mm.

The effect of aqueous garlic extract

The effect of various concentrations of aqueous garlic extract (AGE) on 12 different strains of microorganisms can be shown as below (figure 4)

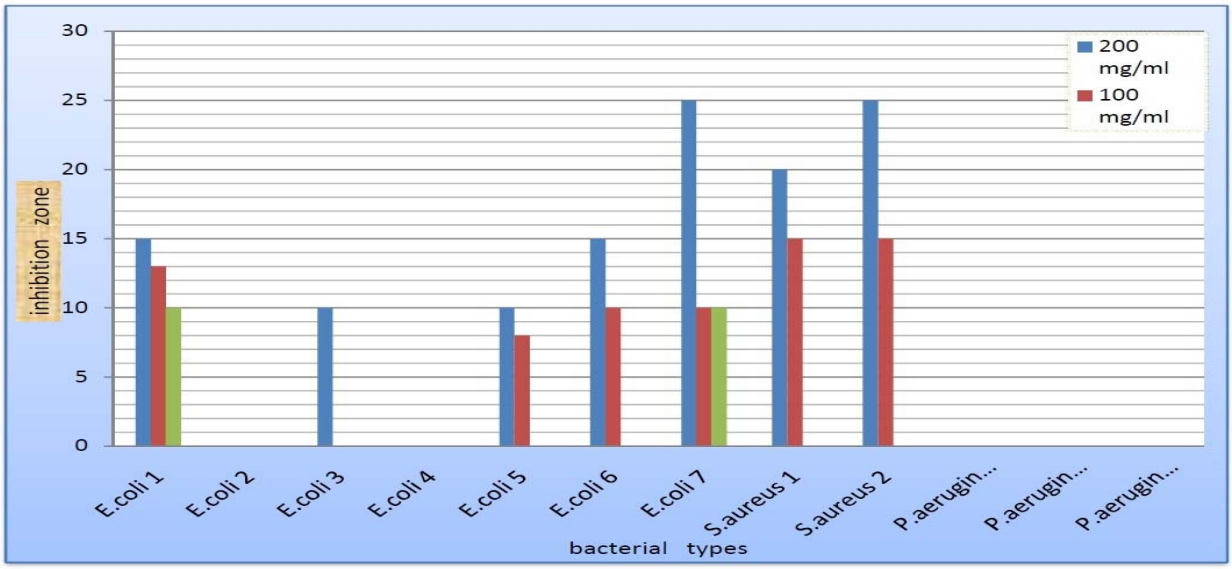

Fig 4: Inhibition effect of aqueous garlic extract against some bacterial strains

The synergistic effect of aqueous garlic extract with antibiotics:

The experiments showed that there was no synergism or synergism of a very low amount between aqueous garlic extract and Am while there was a significant amount of synergism between the aqueous garlic extract and CIP and it could be said that the synergism between these two had the additive effect and the results are as follows:

Table 5: Synergistic effect of AGE with two antibiotics (Am and CIP)

Bacteria	AGE	Am	AGE+Am	CIP	CIP+AGE
E.coli 1	10	R	-	27	40
E.coli 2	R	R	-	35	45
E.coli 3	10	R	-	26	40
E.coli 4	R	12	12	30	35
E.coli 5	8	R	-	20	43
E.coli 6	10	R	-	30	45
E.coli 7	10	10	20	35	40
P.aeruginosa 1	R	R	-	25	40
P.aerugiosa 2	R	R	-	40	40
P.aeruginosa 3	R	R	-	30	40
S.aureus 1	15	15	-	30	45
S.aureus 2	15	15	-	30	45

AGE=Aqueous Garlic Extract Am=Ampicillin CIP=Ciprofloxacin

The action on the ***E.coli*** appeared to be same or more than the summation of

Table 5 &Fig. 5(B). As for the ***Staphylococcus aureus*** isolates the effect was additive which means the effect of the AGE and the CIP was equal to the summation of their effect together (Table5 & Fig. 6B). On the other hand isolates 1&3 of *Pseudomonas aeruginosa* were resistant to the AGE, but it is strength the inhibitory effect of the ciprofloxacin (by increasing the inhibition zone of CIP from 25-40mm for *Pseudomonas aeruginosa 1* and from 30-40mm for *Pseudomonas aeruginosa 3* without any antagonistic effect (table 5 and figure 7b.)

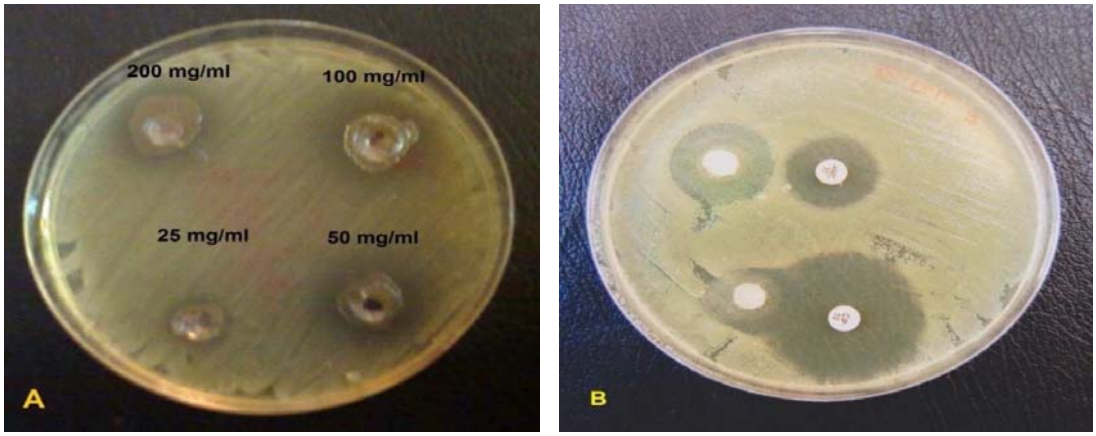

Fig 5 A: The effect of aqueous garlic extract on *E.coli,* B: The effect of aqueous garlic extractand CIP on *E.coli*

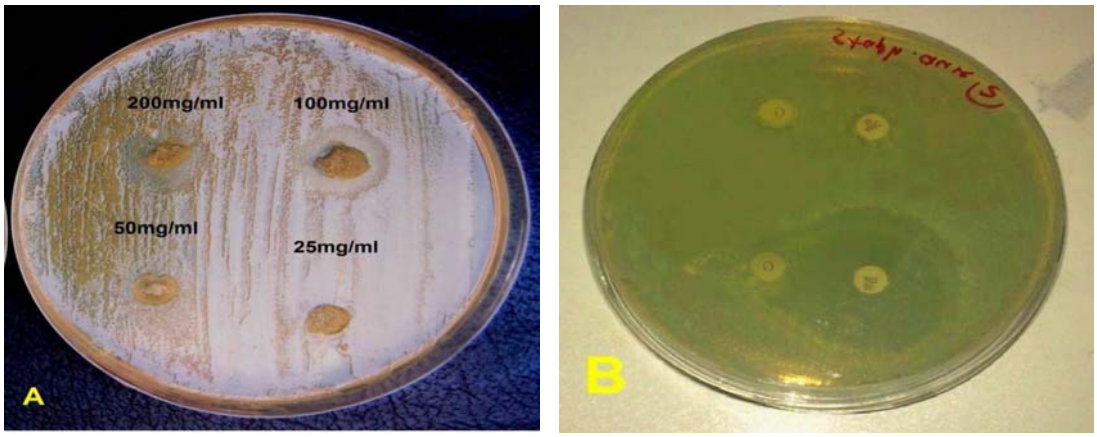

Fig 6 A: The effect of aqueous garlic extract on *S.aureus,* B: The effect of aqueous garlic extract and CIP on *S.aureus*

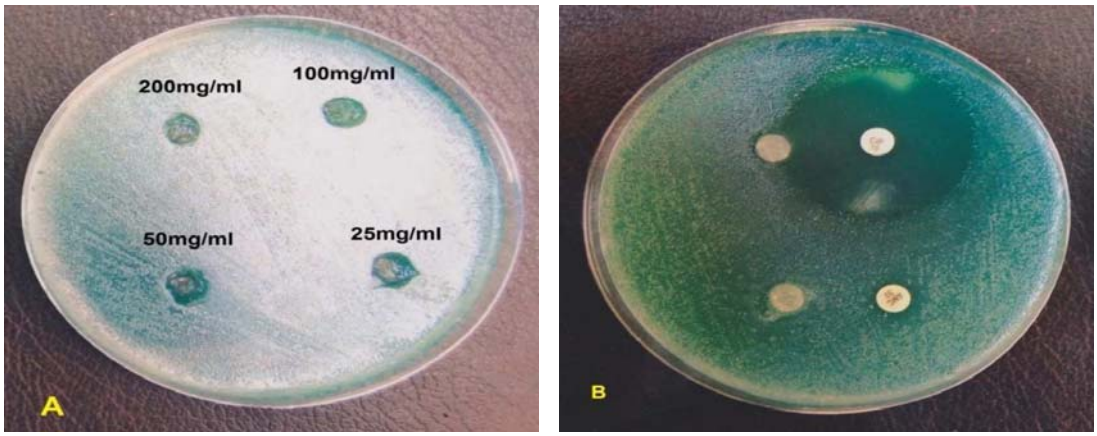

Fig 7 A: The effect of aqueous garlic extract on *P. aeruginosa,* B: The effect of aqueous garlic extractand CIP on *P.aeruginosa*

Discussion

The above mentioned studies clearly tell us about the antimicrobial activities of the various plant products alone as well as along with the other known antibiotics synergistically. And in many cases the effects were additive and showed a proportionate rise in the antimicrobial activity. Though ampicillin does not show synergism to a large extent and it can be said that it has a very little synergism with the plant products being studied whose effect can be neglected if it is to be studied on the real population. And other antibiotics like ciprofloxacin show an exaggerated antimicrobial effect in accordance to the synergism.

Conclusion

Various studies proved that the microorganism are being more resistant to conventional medicines as the amount of doses deliver to the patients is increasing which results in more side effects and to avoid these effects pharmaceuticals should consider the benefits of synergistic effects of traditional and conventional medicines, It is evident from whole of the review above that there are many plant products that have an antimicrobial activity. This antimicrobial potency of these plant products can be increased when they are used with other known antibiotics. It is also seen that many pharmaceutical companies have started using plant products in their products. And it is also appreciated to use such plant products in the conventional medicines. Moreover they do not have any side effects on the human body. And the use of plant products is well accepted wherever there is a possibility of using these plant products nowadays.

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