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Potentiation of Antibacterial Activity of cefixme in Synergy with *Cirsium arvense* (L.) scop. against Resistant Bacterial Isolates

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INTRODUCTION & AIM

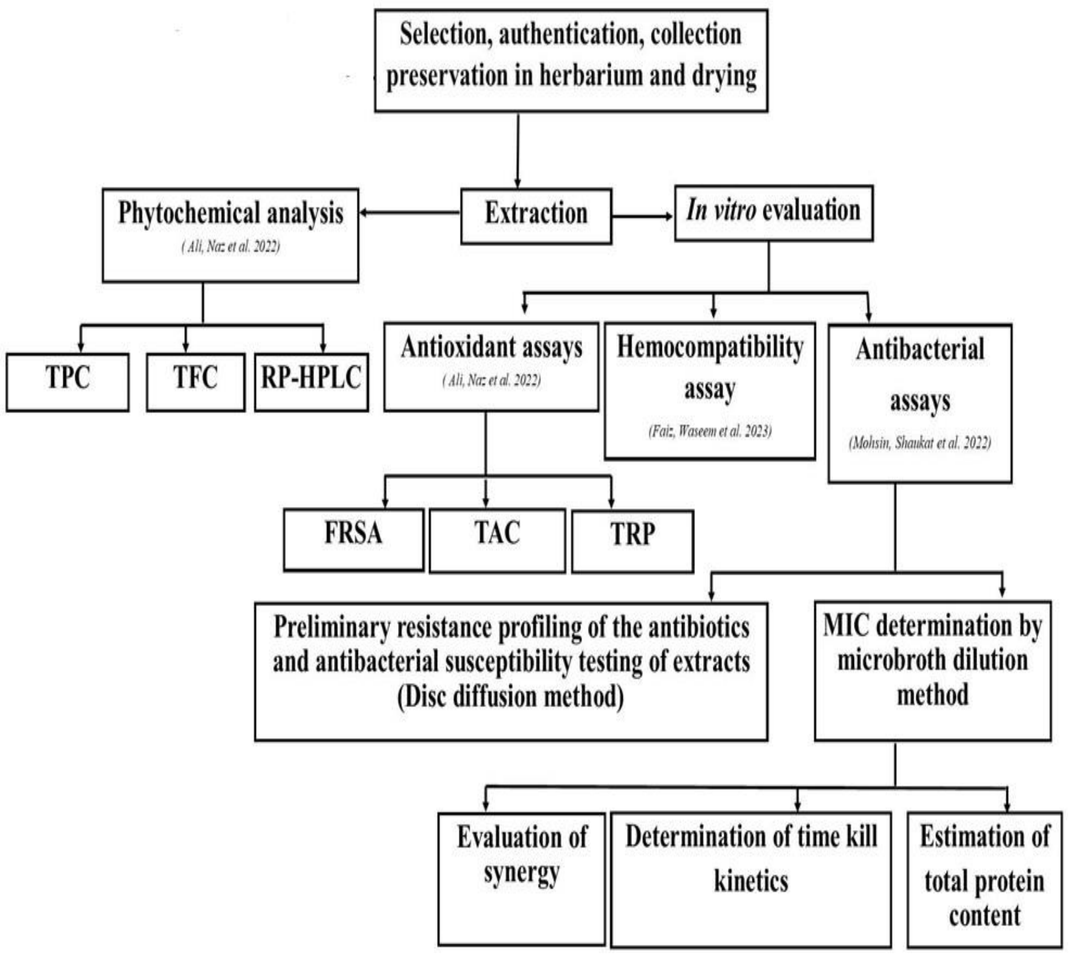
Background: Multidrug resistant bacteria are becoming increasingly prevalent due to irrational use of antibiotics and emergence of new infectious diseases *(Faiz, S., et al, 2023)*. Therefore, it necessitates the development of alternate therapy or new antibiotics.
One of the most crucial tactics for combating bacterial resistance to multiple drugs is the use of antibacterial combinations or treatment with two or more antibacterial agents *(Reygaert and W. C. J. A. M, 2018)* .
Plants have recently been discovered to be synergistic enhancers, meaning that they may resensitize the resistant antibiotics and reduce the doses of antibiotics to several folds *(Bisht V., et al, 2020)*

Aim: Evaluation of the synergistic potential of *Cirsium arvense* extracts with cefixime to combat bacterial resistance.

Objectives:

1. To assess the effect of plant extracts on the growth of resistant strains.
2. To determine whether plant extracts could potentially have greater effect when used with antibiotics that bacterial strains were resistant to.

METHOD



Where TPC stands for total phenol content, TFC stands for total flavonoid content and RP-HPLC stands reverse phase high performance liquid chromatography.
FRSA stands for free radical scavenging activity, TRP stands for total reducing power.

Acknowledgement

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RESULTS & DISCUSSION

Table 1. PROFILING OF ANTIBIOTICS AGAINST RESISTANT ISOLATES

Antibiotics	Diameter of zone of inhibition (ZOI) (mm ± S.D.)		
	R. *E. coli*	*R. Acinetobacter*	MRSA
Doxycycline	17 ± 0.1	21 ± 0.76	28 ± 0.11
Clarithromycin	30 ± 0.3	17 ± 0.23	25 ± 0.1
Lincomycin	21 ± 0.3	14 ± 0.5	20 ± 0.01
Cefixime	NA	NA	NA
Ciprofloxacin	30 ± 0.6	28 ± 0.1	30 ± 0.12

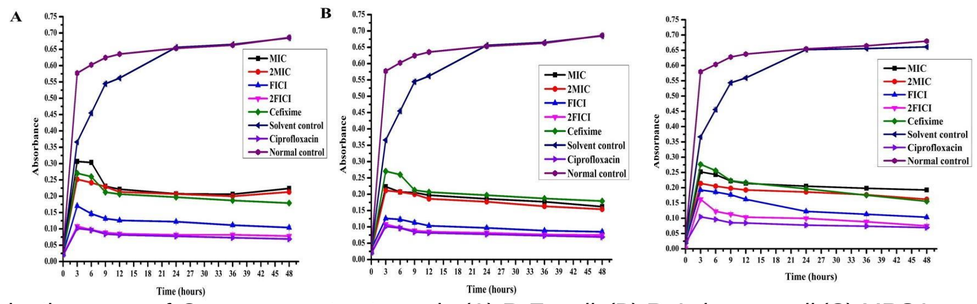
Table 2. PROFILING OF EXTRACTS AGAINST RESISTANT STRAINS

Extract code	The sensitivity pattern zone of inhibition of extracts and standard drugs against test bacterial isolate (ZOI mm ± S.D.)		
	R. MRSA	R. *E. Coli*	R. *A. baumannii*
Cirsium arvense – Ethyl acetate	10 ± 0.2	NA	12 ± 0.7
Cirsium arvense - Methanol	11 ± 0.7	NA	10 ± 0.5
Cirsium arvense - Aqueous	9 ± 0.3	10 ± 0.4	9 ± 0.3
Cefixime	NA	NA	NA
Ciprofloxacin	28 ± 0.06	30 ± 0.12	30 ± 0.12
DMSO	NA	NA	NA

Table 3. SYNERGISTIC INTERACTIONS OF *C. arvense* EXTRACTS

Test Samples	MIC alone	MIC combination	Fold Reduction	FICI	Interpretation
CAEA + Cef	500	62.5	8	0.2	Total Synergism
	100	6.25	16		
CAM + Cef	500	250	4	0.6	Additive
	100	12.5	8		
CAAq + Cef	500	125	2	0.3	Total Synergism
	100	6.25	8		

Figure 2. TIME KILL CURVE FOR DIFFERENT RESISTANT STRAINS



Time-kill kinetics curve of *C. arvense* extracts again (A) R.*E. coli*, (B) R.*A. baumannii* (C) MRSA
Where violet is normal control, navy blue is solvent control, purple is ciprofloxacin, green is MIC of Cefixime, black is 1x MIC of extract, red is 2x MIC of extract, light blue is 1x FICI, and pink is 2x FICI. The results were statistically significant with p-value < 0.05.

CONCLUSION

In vitro evaluation proved that aqueous extract of *Cirsium arvense* is a good candidate demonstrating the highest efficacy in synergy with cefixime against the resistant bacterial isolates as evident from results of time kill kinetics, checkerboard method and protein estimation.
This work could serve as a foundation for developing plant-based antibacterial platforms, utilizing *Cirsium arvense* extracts in synergy with cefixime for combating resistant bacterial pathogens.

FUTURE WORK

Identification and isolation of lead compounds that contribute to the activity
Preclinical *in vivo* research to validate outcomes of obtained *in vitro*
Establishment of mechanism of action