Conclusion
CONCLUSION

Antibiotics are effectively used for the treatment of various bacterial infections. However, they themselves carry risks of adverse side effects. Nephrotoxicity is one such cause of concern in clinical practice, associated with usage of aminoglycosides. Besides there is no consensus of the fact or opinion concerning the primary mechanism responsible for the pathophysiologic manifestation of acute renal failure. ARF is a process in which the kidneys stop their excretory function and it manifests by increase in serum urea and creatinine levels.

Animal studies have shown that different antibiotic induce nephrotoxicity which is dose related i.e. each antibiotic – tobramycin, gentamicin, streptomycin, amikacin and kanamycin included in the study result in profound alterations on the metabolism and functions of kidney which depends on their dosage as well as time (days) of exposure. The doses patterns for different antibiotics included in the study are: tobramycin - 160 mg/kg body weight/day for 12 days; gentamicin - 100 mg/kg body weight/day for 10 days; streptomycin - 300 mg/kg body weight/day for 10 days; amikacin - 250 mg/kg body weight/day for 8 days; kanamycin – 200 mg/kg body weight/day for 8 days. Thus, rats were given above doses of particular aminoglycoside for a particular period of time to induce maximum renal damage, as given by an elevated levels (two fold increase) of serum urea, creatinine and cholesterol together with loss of functional renal marker enzymes i.e. AIP and AcP. Besides kidney these drugs also effected other organs like heart and liver, as is given by hypercholesterolemia and a significant rise in serum transaminases associated with the use of these antibiotics. Besides, antioxidant defence system was also effected as is shown by decrease in the levels of free radical scavenging enzymes i.e. CAT, SOD and GST. To gain an insight into the reversal of nephrotoxic effects of these drugs, fish oil and olive oil were given orally to examine the possible protective role of these oils on various organs of
the rats. Fish oil administration in nephrotoxic rats gave an improvement in the damaged tissues as indicated by normal level of serum urea, creatinine, cholesterol, inorganic phosphate and transaminases. Post fish oil treatment was found to be most effective in bringing the reversal of tobramycin induced nephrotoxicity as is given by normalized levels of serum metabolites studied whereas the pretreatment of fish oil showed less significant effect. However, in case of gentamicin, streptomycin, amikacin and kanamycin, coadministration of fish oil gave a maximum attenuation of the induced damage. However, this difference in beneficial modes of treatment among tobramycin and all other included antibiotics could not be explained. Such modes of fish oil treatment also gave a significant restoration of the activities of marker enzymes of renal membrane and lysosomal membrane suggesting the role of fatty acids present in fish oil in restoration of renal membrane structure, thereby its function. Olive oil treatment on the other hand could not bring profound and consistent recovery of different serum metabolites studied, giving an edge of fish oil usage over olive oil administration in prevention of nephrotoxicity.

Fish oil administration also gave a significant increase in the levels of antioxidant enzymes in kidney and liver. This higher antioxidant potential was able to cope with the increased lipid peroxidation associated with fish oil usage. In tobramycin treated rat, post fish oil treatment gave a maximum induction of antioxidant enzymes whereas for gentamicin, streptomycin, amikacin and kanamycin, coadministration of fish oil gave significantly increased antioxidant potential. On the other hand, olive oil treatment was found to lower oxidative stress to some extent which could be probably due to the fact that although some of its components are similar to fish oil which are however, present in much lower concentration (vitamin E).

The study was further extended to find the specific components of fish oil responsible for its beneficial profile. Linolenic acid and vitamin E that are present in significant amounts in fish oil, when given as post treatment in tobramycin treated rats, were found to give better protection against
nephrotoxicity suggesting that structural integrity, altered metabolic and functional aspects of renal membrane are regained back. Treatment with linolenic acid or vitamin E alone did not give such recovery effects on the metabolic parameters studied suggesting the synergistic role of n-3 fatty acids and vitamin E (as antioxidant) on renal membrane. Comparative results show that maximum protection was observed in tobramycin, when fish oil was administered after the drug for a week. Coadministration of fish oil in gentamicin treated rats also gave a similar effect in amelioration of changes induced by the antibiotic. Thus, fish oil administration offers a better strategy to combat the toxicity associated with the use of antibiotics, without compromising its antibacterial properties.