CONCLUSION

The clinical and pathological outcome during heart, liver, lung and kidney transplantation as well as autoimmune disease treated with CsA, is the chronic nephrotoxicity. The pathogenesis of CsA nephrotoxicity is multifunctional, including inflammation, apoptosis, fibrosis and transformation of renal proximal tubular cells by the epithelial mesenchymal cells.

Hence the search for a multitargeted drug to mitigate the nephrotoxic effect of CsA is the need of the hour. Terminalia arjuna commonly known as abana and used as cardiotonic for decades in ayurvedha, unani, homeopathic and allopathic, serve as the source for isolation of triterpenoid arjunolic acid. The results of the present study reveal that, AA could be a novel therapeutic agent in targeting the down regulation of oxidative stress, inflammatory and apoptotic pathways.

CsA induced increase in pro apoptotic markers and decrease in antiapoptotic protein were attenuated by arjunolic acid. Hence arjunolic acid has significant potential as a therapeutic intervention for chronic CsA induced nephrotoxicity.
MECHANISTIC PATHWAY ABOUT THE ACTION OF ARJUNOLIC ACID ON CYCLOSPORINE (A) INDUCED NEPHROTOXICITY

CsA

+Cas-3

+IL-6

+Bax,-Bcl2
+ Cyt c.

+Nfkb

Tissue fibrosis

Inflammation

Apoptosis

Oxidative stress

Immunosuppression

Cell death

Nephrotoxicity

AA inhibition
FUTURE PROSPECTUS

Future research should focus on defining the cellular and molecular targets, the optimal time frame and the specific strategies for therapeutic intervention of arjunolic acid on chronic cyclosporine induced nephrotoxicity. The special consideration should be given to optimizing modes of local delivery and target of action of AA, that moderate apoptosis so as to target only specific cell such as renal tubular cells for limited period and limit interference with the process of beneficial apoptosis.