6. Summary & Conclusion

- In the present experiment, possible role of PCA and silymarin were investigation in ARS, OBX and CUMS-induced behavioral, biochemical and neurochemical alterations in rodents.
- Normal mice when administered with PCA and silymarin at various doses by orally did not exhibited significant behavioral changes, suggesting both drugs did not induce any effects in non-depressed condition.
- Animals subjected to ARS, OBX and CUMS stress elicited significant increase in immobility time in FST. PCA, silymarin and fluoxetine treatment significantly attenuated the immobility time in FST.
- The exploratory behavior ambulatory and rearing behavior in OBX were also altered in OFT. PCA, silymarin and fluoxetine treatment significantly exploratory behavior OFT test. However, no significant changes on exploratory behaviors in ARS and CUMS models were observed in OFT.
- Mice exposed to different CUMS paradigms induce significant decreased body weight, and preference to sucrose solution and PCA or silymarin or fluoxetine treatment significantly prevented the decrease in body weight and improved preference to sucrose solution in CUMS.
- ARS, OBX and CUMS exposed animals showed elevation of serum corticosterone; MDA formation, lowering of enzymatic antioxidants namely, SOD and CAT in cerebral cortex and hippocampus which were significantly reversed with PCA and silymarin treatment.
- ARS exposed mice did not exhibit any significant alterations in GSH levels in cerebral cortex and hippocampus. However, OBX and CUMS exposed animals depicted a reduced GSH levels in cerebral cortex and hippocampus which were increased by PCA and silymarin treatment. Fluoxetine did not produce any alterations in OBX model but increased GSH levels in CUMS model.
- Monoamines like 5-HT, DA and NE along with BDNF were reduced significantly in hippocampus and cerebral cortex was augmented subsequently with PCA or silymarin or fluoxetine of OBX rats and CUMS mice.
- OBX subjected rats and CUMS exposed mice elicited significant elevation of inflammatory cytokines, TNF-α and IL-6 in hippocampus and cerebral cortex.
Summary and Conclusion

Treatment with PCA or silymarin or fluoxetine attenuated the elevated inflammatory cytokines, TNF-α and IL-6 in hippocampus and cerebral cortex.

- CPP-a NMDA competitive antagonist attenuated immobility time in FST, similar to that of silymarin (100 mg/kg). The attenuated immobility time in FST was not restored with silymarin in CPP pretreated mice, indicating NMDA receptors are not involved in the antidepressant like activity of silymarin in the present study.

Conclusions

Based on above mentioned facts, it is presumed that the antidepressant like activity of PCA and silymarin thus might be correlated to through alleviation of monoaminergic, BDNF, and attenuation of oxidative stress by modulation of corticosterone response, restoration of antioxidant defense system, and inflammatory cytokines system in cerebral cortex and hippocampus (Fig 5.1). In addition, the attenuated immobility time in FST was not restored with silymarin in CPP pretreated mice, indicating NMDA receptors are not involved in the antidepressant like activity of silymarin in the present study. However, further clinical studies are required to confirm the antidepressant activity of silymarin and PCA for the management of depression and associated mood disorders.
Proposed mechanism of action of antidepressant like actions of PCA and silymarin

**Fig 5.1.** Proposed mechanism of action of antidepressant like actions of PCA and silymarin