Summary
SUMMARY

The effect of *B. monniera* extract on the serotonergic system was investigated, oral administration of BME enhanced the learning and retention of previously acquired information significantly in all behavioural tasks. HPLC analysis showed the presence of bioactive compound in the serum of BME treated rats, which demonstrated the uptake of bacoside into the system. The bioactive compounds in the BME could directly or indirectly interact with neurotransmitter systems to enhance learning and memory. The balanced function of various neurotransmitters such as ACh, 5-HT, GABA and Glu were all reported to involved in the regulation of memory formation. Following BME treatment, the level of 5-HT increased while DA decreased significantly, and the level of ACh was altered. However, the estimated variation was not significant in the level of ACh and Glu. The level of 5-HT was significantly elevated up to PND-37 and was then restored to normal level on PND-53. Interestingly, concomitant up-regulation was recorded in the mRNA expression of serotonin synthesizing enzyme *Tph2* and SERT on PND-29 and PND-37, which was normalised on PND-53. The results suggest that BME treatment significantly enhances the learning and memory in postnatal rats possibly through up-regulating the expression of *Tph2*, 5-HT biosynthesis and its transporter.

Subsequent activation of 5-HT receptors responding to elevated endogenous 5-HT level was examined. Semi-quantitative RT-PCR was used to identify the expression pattern of different 5-HT receptors. The screening profile indicated a notable increase in the 5-HT$_{3A}$ receptor expression after treatment with BME compared to all other receptors (5-HT$_{1A}$, 5-HT$_{2A}$, 5-HT$_{4}$, 5-HT$_{5A}$, 5-HT$_{6}$ and 5-HT$_{7}$). The
up-regulated 5-HT$_{3A}$ receptor may interact with serotonergic system or with other neurotransmitters that is involved in learning and memory. The 5-HT$_{3A}$ agonist mCPBG function has facilitated to gain insight into the specific role of 5-HT$_{3A}$ receptor in hippocampal-dependent learning and its interactions with other neurotransmitters. Furthermore, 5-HT$_{3A}$ receptor agonist mCPBG impaired learning in the passive avoidance task followed by reduction of 5-HT$_{3A}$ receptor expression, 5-HT and ACh levels. Administration of BME along with mCPBG attenuated mCPBG induced behavioural, molecular and neurochemical alterations. Obtained results suggest that BME possibly act on serotonergic system through 5-HT$_{3A}$ receptor to improve the hippocampal-dependent task.

Further, to know the molecular mechanism of activated 5-HT$_{3A}$ receptor on synaptic proteins, loss-of-function was developed by treating with D-gal in adult rats. BME alone treated rats showed significantly improved behavioural performances in contextual-associative learning, increased antioxidant markers and synaptic protein levels as compared to control. Whereas, chronic administration of D-gal for 8 weeks significantly impaired the behavioural performance accompanied by a significant elevation in the level of AGE product than all other groups. Interestingly, upon BME treatment, the D-gal treated rats exhibits improved behavioural performance and significant up-regulation in the activity of anti-oxidant enzymes SOD, GPx and Nrf2 expression accompanied with an elevated level of 5-HT. Better performance in contextual associative learning was associated with concomitant increase in the levels of mRNA and proteins of SYP, SYTI, CaMKII and PSD-95 proteins in the hippocampus. Obtained data suggests that BME attenuates the D-gal induced cognitive deficits by up-regulating the cellular antioxidant defense system regulating ARE via
activation of \textit{Nrf2}. In addition, BME possibly increases the level of neurotransmitters, and synaptic proteins thereby improving the contextual-associative learning. Thus, these findings support the therapeutic efficacy of \textit{B. monniera} to enhance the learning efficiency in general and also to improve the age associated learning impairments.