

## LIST OF FIGURES

Figure No.	Figure caption	Page No.
<b>1.</b>	The schematic diagram of the working hypothesis for the present thesis work.	<b>4</b>
<b>2.</b>	The effect of metformin on the level of expression of Akt (B) and p-Akt (D), and ratio of p-Akt to Akt (E) in liver and pancreas of control and T2DM rats. The blots are representative of Akt (A) and p-Akt (C) in liver and pancreas. The results in the histogram are expressed as the ratio of relative intensity of levels of expression of Akt or p-Akt to $\beta$ -actin.	<b>25</b>
<b>3.</b>	The effect of metformin on the level of expression of cytoplasmic (B) and membranous (D), and ratio of p-membranous to cytoplasmic (E) GLUT-4 in liver and pancreas of control and T2DM rats. The blots are representative of cytoplasmic (A) and membranous (C) GLUT-4 in liver and pancreas. The results in the histogram are expressed as the ratio of relative intensity of levels of expression of cytoplasmic or membranous GLUT-4 to $\beta$ -actin.	<b>26</b>
<b>4.</b>	The effect of metformin on the level of expression of cytochrome-C (B) and caspase-9 (D) in liver and pancreas of control and T2DM rats. The blots are representative of cytochrome-C (A) and caspase-9 (C) in liver and pancreas. The results in the histogram are expressed as the ratio of relative intensity of levels of expression of cytochrome-C or caspase-9 to $\beta$ -actin.	<b>27</b>
<b>5.</b>	The effect of metformin on the level of expression of procaspase-3 (B) and caspase-3 (D), and ratio of caspase-3 to procaspase-3 (E) in liver and pancreas of control and T2DM rats. The blots are representative of procaspase-3 (A) and caspase-3 (C) in liver and pancreas. The results in the histogram are expressed as the ratio of relative intensity of levels of expression of procaspase-3 or caspase-3 to $\beta$ -actin.	<b>28</b>
<b>6.</b>	The effect of metformin on ambulation (A), rearing (B), percentage of time spent in the center (C) and total distance travelled (D) in control and T2DM rats during open field test on day-13.	<b>53</b>
<b>7.</b>	The effect of metformin on number of head-dips (A) and edge-sniffs (B), ratio of head-dip/edge sniff (C), and number of squares crossed (D) in control and T2DM rats during hole-board test.	<b>54</b>
<b>8.</b>	The effect of metformin on percentage entries (A) and time spent (B) into open arm, total arm entries (C) and speed in the whole maze (D) in control and T2DM rats during elevated plus maze test.	<b>55</b>
<b>9.</b>	The effect of metformin on the level of expression of Akt (B) and p-Akt (D), and ratio of p-Akt to Akt (E) in hippocampus (HIP), hypothalamus (HYP), pre-frontal cortex (PFC) and amygdale (AMY) of control and T2DM rats. The blots are representative of Akt (A) and p-Akt (C) in HIP, HYP, PFC and AMY. The results in the histogram are expressed as the ratio of relative intensity of levels of expression of Akt or p-Akt to $\beta$ -actin.	<b>56</b>
<b>10.</b>	The effect of metformin on the level of expression of cytoplasmic (B) and membranous (D), and ratio of p-membranous to cytoplasmic (E) GLUT-4 in HIP, HYP, PFC and AMY of control and T2DM rats. The blots are	<b>57</b>

	representative of cytoplasmic (A) and membranous (C) GLUT-4 in HIP, HYP, PFC and AMY. The results in the histogram are expressed as the ratio of relative intensity of levels of expression of cytoplasmic or membranous GLUT-4 to $\beta$ -actin.	
<b>11.</b>	The effect of metformin on the level of expression of cytochrome-C (B) and caspase-9 (D) in HIP, HYP, PFC and AMY of control and T2DM rats. The blots are representative of cytochrome-C (A) and caspase-9 (C) in HIP, HYP, PFC and AMY. The results in the histogram are expressed as the ratio of relative intensity of levels of expression of cytochrome-C or caspase-9 to $\beta$ -actin.	<b>58</b>
<b>12.</b>	The effect of metformin on the level of expression of procaspase-3 (B) and caspase-3 (D), and ratio of caspase-3 to procaspase-3 (E) in HIP, HYP, PFC and AMY of control and T2DM rats. The blots are representative of procaspase-3 (A) and caspase-3 (C) in HIP, HYP, PFC and AMY. The results in the histogram are expressed as the ratio of relative intensity of levels of expression of procaspase-3 or caspase-3 to $\beta$ -actin.	<b>59</b>
<b>13.</b>	The effect of metformin on ambulation (A), rearing (B), percentage of time spent in the center (C) and total distance travelled (D) in control and T2DM-induced encephalopathic rats during open field test on day-31.	<b>86</b>
<b>14.</b>	The effect of metformin on number of head-dips (A) and edge-sniffs (B), ratio of head-dip/edge sniff (C), and number of squares crossed (D) in control and T2DM-induced encephalopathic rats during hole-board test.	<b>87</b>
<b>15.</b>	The effect of metformin on percentage entries (A) and time spent (B) into open arm, total arm entries (C) and speed in the whole maze (D) in control and T2DM-induced encephalopathic rats during elevated plus maze test.	<b>88</b>
<b>16.</b>	The effect of metformin on the level of expression of Akt (B) and p-Akt (D), and ratio of p-Akt to Akt (E) in hippocampus (HIP), hypothalamus (HYP), pre-frontal cortex (PFC) and amygdale (AMY) of control and T2DM-induced encephalopathic rats. The blots are representative of Akt (A) and p-Akt (C) in HIP, HYP, PFC and AMY. The results in the histogram are expressed as the ratio of relative intensity of levels of expression of Akt or p-Akt to $\beta$ -actin.	<b>89</b>
<b>17.</b>	The effect of metformin on the level of expression of cytoplasmic (B) and membranous (D), and ratio of p-membranous to cytoplasmic (E) GLUT-4 in HIP, HYP, PFC and AMY of control and T2DM-induced encephalopathic rats. The blots are representative of cytoplasmic (A) and membranous (C) GLUT-4 in HIP, HYP, PFC and AMY. The results in the histogram are expressed as the ratio of relative intensity of levels of expression of cytoplasmic or membranous GLUT-4 to $\beta$ -actin.	<b>90</b>
<b>18.</b>	The effect of metformin on the level of expression of cytochrome-C (B) in HIP, HYP, PFC and AMY of control and T2DM-induced encephalopathic rats. The blots are representative of cytochrome-C (A) in HIP, HYP, PFC and AMY. The results in the histogram are expressed as the ratio of relative intensity of levels of expression of cytochrome-C to $\beta$ -actin.	<b>91</b>
<b>19.</b>	Flow cytogram showing cell death assessed by cytometric analysis using annexin-V/PI. Dot plots are representative for HIP, HYP, PFC and AMY of	<b>92</b>

	control (A), MET (B), T2DM (C) and DMET (D).	
<b>20.</b>	The effect of metformin on the percentage in apoptotic cells in HIP, HYP, PFC and AMY of control and T2DM-induced encephalopathic rats.	<b>93</b>
<b>21.</b>	Effect of muscimol in presence/absence of bicuculline or wortmannin on T2DM-induced changes in the level of hepatic intracellular calcium.	<b>110</b>
<b>22.</b>	The effect of muscimol in presence/absence of bicuculline or wortmannin on the level of expression of Akt (B) and p-Akt (C), and ratio of p-Akt to Akt (D) in liver of T2DM rats. The blots are representative of Akt and p-Akt in liver (A). The results in the histogram are expressed as the ratio of relative intensity of levels of expression of Akt or p-Akt to $\beta$ -actin.	<b>111</b>
<b>23.</b>	The effect of muscimol in presence/absence of bicuculline or wortmannin on the level of expression of cytoplasmic (B) and membranous (C), and ratio of p- membranous to cytoplasmic (D) GLUT-4 in liver of T2DM rats. The blots are representative of cytoplasmic and membranous (A) GLUT-4 in liver. The results in the histogram are expressed as the ratio of relative intensity of levels of expression of cytoplasmic or membranous GLUT-4 to $\beta$ -actin.	<b>112</b>
<b>24.</b>	Effect of metformin in presence/absence of bicuculline or wortmannin on T2DM-induced changes in the level of hepatic intracellular calcium.	<b>129</b>
<b>25.</b>	The effect of metformin in presence/absence of bicuculline or wortmannin on the level of expression of Akt (B) and p-Akt (C), and ratio of p-Akt to Akt (D) in liver of T2DM rats. The blots are representative of Akt and p-Akt in liver (A). The results in the histogram are expressed as the ratio of relative intensity of levels of expression of Akt or p-Akt to $\beta$ -actin.	<b>130</b>
<b>26.</b>	The effect of metformin in presence/absence of bicuculline or wortmannin on the level of expression of cytoplasmic (B) and membranous (C), and ratio of p- membranous to cytoplasmic (D) GLUT-4 in liver of T2DM rats. The blots are representative of cytoplasmic and membranous (A) GLUT-4 in liver. The results in the histogram are expressed as the ratio of relative intensity of levels of expression of cytoplasmic or membranous GLUT-4 to $\beta$ -actin.	<b>131</b>
<b>27.</b>	The effect of VS and time-dependent exposure of first RS on immobility period in FST in rats.	<b>151</b>
<b>28.</b>	The effect of VS and time-dependent exposure of first RS on percentage of open arm entries (A), time spent (B), and total arm entries (C) in rats.	<b>152</b>
<b>29.</b>	The effect of VS and time-dependent exposure of first RS on the total arm entries in trial-1 and 2 (curiosity; A), spatial recognition memory (B) and coping behavior to novel arm (anxiety-like behavior; C) in Y-maze test paradigm.	<b>153</b>
<b>30.</b>	The effect of VS and time-dependent exposure of first RS on the plasma level of ACTH and corticosterone in rats.	<b>154</b>
<b>31.</b>	The effect of VS and time-dependent exposure of first RS on the level of expression of CRH-1(B) and CRH-2 (D) in HIP, HYP, PFC and AMY of rats. The blots are representative of CRH-1 (A) and CRH-2 (B) in HIP, HYP, PFC and AMY. The results in the histogram are expressed as the ratio of relative intensity of levels of expression of CRH-1 or CRH-2 to $\beta$ -actin.	<b>155</b>

<b>32.</b>	The effect of VS and time-dependent exposure of first RS on the level of expression of Akt (B) and p-Akt (D), and ratio of p-Akt to Akt (E) in HIP, HYP, PFC and AMY of rats. The blots are representative of Akt (A) and p-Akt (C) in HIP, HYP, PFC and AMY. The results in the histogram are expressed as the ratio of relative intensity of levels of expression of Akt or p-Akt to $\beta$ -actin.	<b>156</b>
<b>33.</b>	The effect of VS and time-dependent exposure of first RS on the level of expression of MR (B) and GR (D), and ratio of MR to GR (E) in HIP, HYP, PFC and AMY of rats. The blots are representative of MR (A) and GR (C) in HIP, HYP, PFC and AMY. The results in the histogram are expressed as the ratio of relative intensity of levels of expression of MR or GR to $\beta$ -actin.	<b>157</b>
<b>34.</b>	Representative figures for mitochondrial respiration pattern in HIP (A), HYP (B), PFC (C) and AMY (D) of control and PTSD-like rats.	<b>158</b>
<b>35.</b>	The effect of sertraline (0.1, 1.0 and 10.0 mg/kg) on SRS-induced changes in the immobility period in FST.	<b>189</b>
<b>36.</b>	The effect of sertraline (0.1, 1.0 and 10.0 mg/kg) on SRS-induced changes in the percentage open arm entries (A), time spent (B) and total arm entries (C) in EPM.	<b>190</b>
<b>37.</b>	The effect of SER (0.1, 1.0 and 10.0 mg/kg) on the total arm entries in trial-1 and 2 (curiosity; A), spatial recognition memory (B) and coping behavior to novel arm (anxiety-like behavior; C) in Y-maze test paradigm.	<b>191</b>
<b>38.</b>	The effect of SER (0.1, 1.0 and 10.0 mg/kg) on the SRS-induced changes in Bmax (A) and Kd (B) for 5-HT <sub>1A</sub> and Bmax (C) and Kd (D) for 5-HT <sub>2A</sub> in HIP, HYP, PFC and AMY of rats.	<b>192</b>
<b>39.</b>	Representative figures for mitochondrial respiration pattern in HIP (A), HYP (B), PFC (C) and AMY (D) of control, SRS and SER (0.1, 1.0 and 10.0 mg/kg) treated PTSD-like rats.	<b>193</b>
<b>40.</b>	The effect of SER (0.1, 1.0 and 10.0 mg/kg) on the SRS-induced changes in RCR (A) and ADP/O (B) in HIP, HYP, PFC and AMY of rats.	<b>194</b>
<b>41.</b>	The effect of SER (0.1, 1.0 and 10.0 mg/kg) on the level of expression of Akt (C) and p-Akt (D), and ratio of p-Akt to Akt (E) in HIP, HYP, PFC and AMY of control and T2DM rats. The blots are representative of Akt (A) and p-Akt (B) in HIP, HYP, PFC and AMY. The results in the histogram are expressed as the ratio of relative intensity of levels of expression of Akt or p-Akt to $\beta$ -actin.	<b>195</b>
<b>42.</b>	The effect of SER (0.1, 1.0 and 10.0 mg/kg) on the level of expression of cytoplasmic (C) and membranous (D), and ratio of membranous to cytoplasmic (E) GLUT-4 in HIP, HYP, PFC and AMY of SRS rats. The blots are representative of cytoplasmic (A) and membranous (B) GLUT-4 in HIP, HYP, PFC and AMY. The results in the histogram are expressed as the ratio of relative intensity of levels of expression of cytoplasmic or membranous GLUT-4 to $\beta$ -actin.	<b>196</b>
<b>43.</b>	The effect of metformin (MET), diazepam (DZ) and their combination on gastric ulcer in T2DM and repeated CRS paradigm (DMS) exposed rats.	<b>219</b>
<b>44.</b>	The effect of MET, DZ and their combination on DMS-induced alterations in percentage of open arm entries to total arm entries (A), percentage of	<b>220</b>

	open arm time spent to total arm time spent (B), and total arm entries (C) in EPM.	
<b>45.</b>	The effect of MET, DZ and their combination on DMS-induced changes in the level of expression of phospho-IRS <sup>ser307</sup> (p-IRS <sup>ser307</sup> ) and total IRS in the liver tissues. The blots are representative of p-IRS <sup>ser307</sup> and total IRS (A) in the liver tissues. The results in the histogram are expressed as ratio of relative intensity of levels of protein expression of either p-IRS <sup>ser307</sup> or total IRS to $\beta$ -actin, and ratio of relative intensity of level of expression of p-IRS <sup>ser307</sup> to total IRS.	<b>221</b>
<b>46.</b>	The effect of MET, DZ and their combination on DMS-induced changes in the level of expression of phospho-Akt <sup>ser473</sup> (p-Akt <sup>ser473</sup> ) and total Akt in the liver tissues. The blots are representative of p-Akt <sup>ser473</sup> and total Akt (A) in the liver tissues. The results in the histogram are expressed as ratio of relative intensity of levels of protein expression of either p-Akt <sup>ser473</sup> or total Akt to $\beta$ -actin, and ratio of relative intensity of level of expression of p-Akt <sup>ser473</sup> to total Akt.	<b>222</b>
<b>47.</b>	The effect of MET, DZ and their combination on mitochondrial succinate dehydrogenase (SDH) activity and membrane potential in discrete brain regions in DMS exposed rats.	<b>223</b>
<b>48.</b>	The effect of MET, DZ and their combination on mitochondrial lipid peroxidation (LPO), and superoxide dismutase (SOD) and catalase (CAT) activities in discrete brain regions in DMS exposed rats.	<b>224</b>
<b>49.</b>	The effect of metformine, sertraline and their combination on SRS-induced changes in the immobility period in FST.	<b>250</b>
<b>50.</b>	The effect of metformin, sertraline and their combination on SRS-induced changes in the percentage open arm entries (A), time spent (B) and total arm entries (C) in EPM.	<b>251</b>
<b>51.</b>	The effect of MET, SER and their combination on DMP-induced changes in the total arm entries in trial-1 and 2 (curiosity; A), spatial recognition memory (B) and coping behavior to novel arm (anxiety-like behavior; C) in Y-maze test paradigm.	<b>252</b>
<b>52.</b>	The effect of MET, SER and their combination on DMP-induced changes in the level of expression of 5-HT <sub>2A</sub> (B) in HIP, HYP, PFC and AMY of rats. The blots are representative of 5-HT <sub>2A</sub> (A) in HIP, HYP, PFC and AMY. The results in the histogram are expressed as the ratio of relative intensity of levels of expression of 5-HT <sub>2A</sub> to $\beta$ -actin.	<b>253</b>
<b>53.</b>	The effect of MET, SER and their combination on DMP-induced changes in the level of expression of GABA <sub>A</sub> (B) in HIP, HYP, PFC and AMY of rats. The blots are representative of GABA <sub>A</sub> (A) in HIP, HYP, PFC and AMY. The results in the histogram are expressed as the ratio of relative intensity of levels of expression of GABA <sub>A</sub> to $\beta$ -actin.	<b>254</b>
<b>54.</b>	The effect of MET, SER and their combination on DMP-induced changes in the intracellular Ca <sup>+2</sup> in discrete brain regions.	<b>255</b>
<b>55.</b>	The effect of MET, SER and their combination on DMP-induced changes in the RCR (A), ADP/O (B) and MMP (C) in discrete brain regions.	<b>256</b>
<b>56.</b>	The effect of MET, SER and their combination on the level of expression of	<b>257</b>

	Akt (C) and p-Akt (D), and ratio of p-Akt to Akt (E) in HIP, HYP, PFC and AMY of control and T2DM rats. The blots are representative of Akt (A) and p-Akt (B) in HIP, HYP, PFC and AMY. The results in the histogram are expressed as the ratio of relative intensity of levels of expression of Akt or p-Akt to $\beta$ -actin.	
<b>57.</b>	The effect of MET, SER and their combination on DMP-induced changes in the level of expression of cytoplasmic (C) and membranous (D), and ratio of membranous to cytoplasmic (E) GLUT-4 in HIP, HYP, PFC and AMY of rats. The blots are representative of cytoplasmic (A) and membranous (B) GLUT-4 in HIP, HYP, PFC and AMY. The results in the histogram are expressed as the ratio of relative intensity of levels of expression of cytoplasmic or membranous GLUT-4 to $\beta$ -actin.	<b>258</b>
<b>58.</b>	The overt outcome of the combination of specific objectives of the thesis work.	<b>265</b>