A comparative study of the effects of esculetin, esculin and 4-methylesculetin in acute experimental model of inflammatory bowel disease

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Introduction: Esculetin, esculin and 4-methylesculetin are coumarin derivatives known to have antioxidant and anti-inflammatory activity. Esculetin and 4-methylesculetin present beneficial effects in experimental model of inflammatory bowel disease (IBD) and it is known that esculin is converted to esculetin in the cells. Based on this, the aim of this study was to compare the effects of these coumarins in acute experimental model of rat colitis.

Materials and Methods: Rats (n=8) were treated (p.o.) with esculetin (5mg/Kg), esculin (25mg/Kg), 4-methylesculetin (5mg/Kg) and azathioprine (2mg/Kg), sulfasalazine (50mg/Kg), prednisolone (2mg/Kg), the reference drugs used for IBD treatment, at 96, 72, 48, 24 and 2 hours before the colitis induction by trinitrobenzenesulfonic acid (TNBS). The animals were killed 48 h after colitis induction and the macroscopic and biochemical parameters (mieloperoxidase (MPO), TNF-α and INF-γ) were evaluated, (Protocol 042/04-CEEA).

Results/Discussion: 4-methylesculetin promoted a reduction in 31.25% in macroscopic score, 44.68% in extension of lesion, 77.28% in incidence of diarrhea and 57.15% in adherence and promoted a reduction in 32.21% in MPO activity. Esculin promoted a reduction in 24.78% in MPO activity, and esculetin did not promote any alteration in the analyzed parameters. Azathioprine and sulfasalazine promoted a reduction in 45.27 and 33.72% in MPO activity respectively.

Conclusion: Preliminary results demonstrated that 4-methylesculetin present better effect than esculetin, esculin and reference drugs. These results suggest that the presence of methyl group in carbon C-4 of the esculetin structural molecule increased the anti-inflammatory effects of the coumarins, promoting an improvement of intestinal inflammatory process. Comparatively, 4-methylesculetin might be interesting as a new anti-inflammatory compound used for the prevention of inflammatory bowel disease.

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