mRNA expression in mice treated with Aβ42 compared to controls, while BCRP expression was not affected. These findings indicate that, in addition to the age-related decrease of Pgp expression, Aβ42 itself downregulates the expression of Pgp and other Aβ-transporters, which could exacerbate the intracerebral accumulation of Aβ and thereby accelerate the neurodegeneration and cerebral Aβ angiopathy.(93)
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And

Plan of work

Research envisaged and the plan of research work:

Stress is the most common problem of today's world. As per current report of “Stress in America” the U.S. economy continues to struggle for the third year. Findings from the 2010 Stress in America survey paint a picture of an overstressed nation. Survey findings consistently show that today, the majority of people are living with moderate stress (4 – 7 on a scale of 1 to 10, where 1 means you have little or no stress and 10 means you have a great deal of stress) or high (8 – 10 on a scale of 1 to 10) levels of stress. (94)

Men and women report different reactions to stress, both physically and mentally and they attempt to manage stress in very different ways. Findings suggest that women are more likely to report physical symptoms associated with stress than men and it is on continuous rise. (94)

As of now, no specific treatment of stress is available, although there are number of disorders associated with stress, most common of them are
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depression, ulceration and infertility, dementia and alzheimer’s disease. A number of synthetic molecules are available in the market for the treatment of stress and the stress induced disorders. Undoubtedly, such synthetic molecules are effective in the treatment of but such chemical entities possesses potential side effects which may induce cellular damage. (94, 95)

It is necessary to mention this fact that the potential antioxidant activity of M. pruriens and H. perforatum may serve a protective effect on stress induced ulceration, depression and sexual deficiency. Apart from this, to avoid the side effects associated with the available synthetic drugs and the to generate an efficient therapy, the 50% MeOH extract of M. pruriens and H. perforatum were selected which possesses significant activity against stress induced disorders. Such stress induced disorders are regulated by efflux transporter protein localized at the membrane of gastric mucosa, testicular cell membrane and brain endothelial cells.(30)

Pgp regulates the movement of drugs and xenobiotics across the gastric mucosal membrane, blood-testis barrier and blood-brain barrier and prevent the cellular damage. Hence, the up-regulation of Pgp prevent the proliferation of ulceration, depression and sexual deficiency. The expression of key efflux transporter, Pgp at the luminal surface of gastric mucosal membrane, blood-testis barrier and blood-brain barrier is regulated by the Wnt/β-catenin signalling pathway. A direct regulation of Wnt/β-catenin pathway regulates the expression of Pgp which efflux out and inhibits the entry of the toxicants, free radicals and xenobiotics across the cell membrane and hence inhibit ulceration, depression and infertility.(94, 95)(30)

Based on the reviewed literature, the well known medicinal herbs M. Pruriens and H. Perforatum were selected for the treatment of stress induced
ulceration, depression and sexual deficiency with a specific target to generate an efficient and safe treatment of stress induced disorders.

Plan of research work

The research investigation involved the following studies

1. **Collection and authentication of seeds of M. pruriens and aerial portion of H. perforatum**
2. **Processing of drugs for defatting and successive extraction**
3. **Bioassay and TLC guided selection of extracts for -**
   3.1 Antioxidant bioassay
      3.1.1 DPPH inhibition
      3.1.2 Free radical scavenging activity
4. **Dose design and toxicity studies of extracts**
   4.1 Morphological evaluation of GC-2 and hCMEC/D3 cells and evaluation of IC₅₀
   4.2 Measurement of DNA damage
   4.3 Measurement of apoptotic index
   4.4 Cell viability study
5. Effect of stress (Cold stress, tail suspension stress, forced swim stress, learned helplessness stress and immobilization stress) on –

5.1 Behavior of animals for sexual deficiency
   5.1.1 Mount latency (ML)
   5.1.2 Intromission latency (IL)
   5.1.3 Ejaculation latency (EL)
   5.1.4 Mount frequency (MF)
   5.1.5 Intromission frequency (IF)
   5.1.6 Ejaculation frequency (EF)
   5.1.7 Penile erection index (PEI)

5.2 Estimation of Blood and gastric parameters for ulceration
   5.2.1 Alkaline phosphatase (ALP) estimation
   5.2.2 Amylase estimation
   5.2.3 Albumin estimation
   5.2.4 Glucose estimation
   5.2.5 Blood urea nitrogen (BUN) estimation
   5.2.6 Cholesterol estimation
   5.2.7 Creatinine estimation
   5.2.8 Triglyceride estimation
   5.2.9 Estimation of gastrin
   5.2.10 Estimation of somatostatin

5.3 Estimation of Neurotransmittersto assess depression by
   5.3.1 Epinephine estimation
   5.3.2 Norepinephrine estimation
   5.3.3 Dopamine estimation
   5.3.4 Glycine estimation
   5.3.5 Glutamate estimation
   5.3.6 GABA estimation
   5.3.7 Estimation of 5-hydroxy tryptamine