2. **Hypothesis**

RA is an autoimmune disease that involves inflammation of the synovium with progressive erosion of bone, leading in most cases to misalignment of the joint, loss of function, and disability. Most of the patients with rheumatoid arthritis were treated according to a sequential strategy, beginning with a nonsteroidal anti-inflammatory drug. Nonsteroidal anti-inflammatory drugs (NSAIDs) commonly used in RA treatment are ibuprofen, etoricoxib, nabumetone and naproxen. The people suffering from chronic pain in RA and those dissatisfied with current treatment are very likely to seek alternative treatments, and an estimated 60–90% of persons with arthritis use CAM (traditional or complementary and alternative medicine).

*Andrographis paniculata* (Acanthaceae) commonly known as king of bitters is a frequently used herb in Ayurvedic formulations and has several biological activities including hepatoprotective, antioxidant, antivenom, antifertility, inhibition of replication of the HIV virus, antimalarial, antifungal, antibacterial, antidiabetic, suppression of various cancer cells and principally anti-inflammatory properties. Andrographolide is one of the active constituent of *Andrographis paniculata Nees* (AP) and has been reported to have antiarthritic effect.

As per the previous studies, AN induces CYP1A2 activity. According to few literature, AN inhibits CYP1A2. APE has CYP1A2 inhibitory activity *in vitro*. ETO is predominantly (60 %) metabolized by CYP3A4 in humans and also by CYP1A2, CYP2D6, CYP2C9, and CYP2C19 to lesser extent. As CYP3A4 is not present in rats, the possible pathway of metabolism of ETO in rats may be through CYP1A1 and CYP1A2. CYP1A2 plays an important role in the metabolism of NAB to the active metabolite 6-MNA along with other enzymes like CYP2C6, CYP2C11 in rats and CYP2A6, CYP2C9, CYP19, CYP2D6, CYP3A4 in human. CYP2C9 and CYP1A2 together account for the majority of R- and S-naproxen 0-demethylation in human liver *in vitro* and acts as a substrate in the metabolism of naproxen.

Thus the hypothesis was any substance influencing the CYP1A2 enzyme is likely to affect the metabolism of ETO, NAB and NP, which should be studied.