

Travail dirigé (TD)

Après avoir lu attentivement le texte suivant (non titré), vous répondez aux questions suivantes :

- 1- Trouvez 3 à 4 mots clés appropriés au texte
- 2- Utilisez ces mots clés pour retrouver le texte sur l'internet en mentionnant la revue dans laquelle le texte est publié (Nom de la revue, Volume, Année de publication)
- 3- Indiquez le titre du texte.

Herbal products derived from roots, leaves or bark are the most important components of traditional medicine in West Africa, where traditional healers provide the primary health care for treatment of many diseases (Ewu, 1993). It is estimated, that more than 80% of the population of developing countries use traditional medicines (Bennett and Brown, 2000) to treat many health conditions, despite expansion of allopathic medicine. Self-medication and combination therapy using western medicines and traditional herbal medicines are frequent. Herbal products in Africa are prepared mainly as infusions or decoctions in water or alcohol, and they are administered orally, except those used in the treatment of external conditions such as wounds. Frequently traditional medicines are polyherbal preparations, and it is thought that some of the plants present in a given preparation are used to increase the effectiveness or decrease the potential toxicity effect of others. In particular, some species are repeatedly used in very different traditional medicines and may be described as adjuvant plants. Little scientific evaluation of this possibility has been undertaken. Herbal products may alter the bioavailability of drugs or others xenobiotic compounds, administered orally, which is mainly controlled by cytochrome P450 isozymes present at high levels in the villus tip of enterocytes in the gastrointestinal tract (Zhang et al., 1998; Benet and Cummins, 2001). The human genome encodes for many isoforms of CYP and the most abundant is the CYP3A subfamily that includes the enzyme CYP3A4, CYP3A5 and CYP3A7. CYP3A4 expressed mainly in the human intestine and liver, is involved in the metabolism of greater than 50% of clinically used drugs such as immunosuppressants, calcium antagonists, anti-infectives, non-sedating antihistamine drugs (Venkatakrisnan et al., 2000). Medicinal plants, plant derived food and beverages can modulate

metabolic activity of CYP3A4 as has been demonstrated in published studies. Single-entity herbal product such as golden seal, *Hydrastis canadensis*, black tea (*Camilla sativa*) or herbal mixtures have been demonstrated to strongly inhibit CYP3A4-mediated metabolism in vitro (Foster et al., 2003). Furthermore, simultaneous administration of natural products with medicines that are metabolized by CYP3A enzymes may increase plasma concentration of these medicines and could cause unexpected adverse effects. In previous studies undertaken by Schmiedlin-Ren et al. (1997), it was shown that grapefruit juice induced a decline in intestinal CYP3A4 in vivo and in vitro activity. Intake of St. John's wort extract (*Hypericum perforatum*) induced a biphasic effect where there was inhibition of activity during short-term use and induction of activity after long-term administration (Rengelshausen et al., 2005). CYP3A4 and CYP3A5 account for approximately 30% of total CYP450 human enzyme (Guengerich, 2003). Recent studies have shown that there are ethnic population differences in the expression levels of adult liver CYP3A mRNAs (Yamaori et al., 2005). CYP3A5 is expressed in one-third of Caucasian and over one-half of African-American samples (Kuehl et al., 2001). Based on results obtained by Williams et al. (2002), it was predicted that the metabolic clearance of some of substrates such as midazolam, triazolam, tamoxifen and diltiazem, in the liver in vivo, would be greater for those individuals expressing high level of CYP3A5 compared with those not expressing this enzyme. For example, oral bioavailability of some of immunosuppressants such as cyclosporine, tacrolimus, sirolimus and everolimus in African-American populations was 20–50% lower than in Caucasian populations (Dirks et al., 2004). CYP3A7 is another individual enzyme of 3A subfamily, which is expressed, mainly in fetal liver and in the rare cases in adults. This enzyme has various substrates that are similar to CYP3A4 substrates. Its typical substrates are steroids and barbituric acids (Anzenbacher and Anzenbacherova, 2001). It has been documented that Americans and other populations use herbal products concurrently with prescribed medicines and frequently patients fail to tell their physicians about their use of supplements, and physicians often fail to ask (Huang et al., 2004). This situation is, even more prevalent in African countries in general, where unfortunately, HIV-AIDS and malaria diseases are progressing and kill many millions of people each year. For this reason and many others, such as cultural and social practice, medicinal plants are used intensively and concomitantly with allopathic medicines in the treatment of opportunity diseases. However, there is little information about the interactions between medicines and botanical products used currently in West Africa area. Therefore, it would be useful, for public health programs in

developing countries, to learn more concerning the effect of these plant products on CYP450 enzymes. This first study is designated to evaluate the inhibitory potential of extracts of three groups of plants: medicinal, food and co-administered plants, ingested currently in many West African countries, on the three isoforms of CYP3A enzymes, 3A4, 3A5 and 3A7, to predict potential interactions in vivo with conventional drugs or herbal products. We report that these plants present higher inhibition of CYP3A subfamily than common medicinal plants and food plants, which are ingested frequently and may be selected for their use as pharmacoenhancers.