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REVIEW PAPER

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Plant medicinal products and drug interactions

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ABSTRACT

Introduction. Some herbal medicinal products may be beneficial in certain respects but many can be dangerous for patients taking doctor-prescribed medications. Plant medicinal products are often taken with conventional drugs by patients. Interactions are possible between herbal medicinal products and conventional medications that can lead to toxicity due to increased drug plasma levels or drug treatment failure.

Aim. The aim of the study was to review the study of plant medicinal products and drug interactions.

Materials and method. Analysis of literature.

Keywords. drug interactions, natural products, drug, therapeutic material

Introduction

Synthetic drug interactions with plant-based medicinals can take place in several phases: at the stage of absorption of drugs from the gastrointestinal tract (pharmacokinetic phase), during drug metabolism by cytochrome P-450 enzymes (pharmacokinetic phase).[1-6] Conventional drug and plant medicinals may also exhibit additive and hyperadditional synergism during the pharmacodynamic phase.[7-10] Complications arise if an interaction lessens the intended effect or amplifies an adverse side effect.[11-14]

Disorders in the absorption stage of synthetic drugs are the main cause of therapy failure. Among the plant medicines contributing to this type of interaction of note are flax seeds (Lini semen) and the seeds of the plantago (Plantaginis ovatae semen). The absorption of synthetic drugs from the gastrointestinal tract is also influenced by their mobility through the digestive tract. Herbal laxatives containing extracts of aloe vera, rooting root, buckthorn bark, or senna leaves intensify intestinal passage, leading to a reduced absorption of conventional synthetic drugs.[15-20]

Interactions at the metabolic stage result from the inhibition or activation of cytochrome P-450 enzymes. Clinical St. John's wort (Hyperici herba) is an import-

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ant therapeutic resource that is known to disturb the metabolism of a variety of drugs. The active substances contained in St. John's wort extract include hyperoside, hypericin, and pseudohipericin induce the activity of P-450 type CYP3A4, CYP2C9 and CYP2C19 isoenzymes. As a result of the combined use of drugs that are substrates of these isoenzymes and St John's wort, there is a reduction in the therapeutic concentration of synthetic drugs in the blood. The most dangerous interactions with St John's wort include anticoagulants, immunosuppressants, antivirals (including those used in HIV therapy), non-steroidal anti-inflammatory drugs and statins. Flavonolignans, phytosterols and flavonoids are raw plant-based materials that also cause an increase in CYP3A4 activity. Decreasing the metabolism of drugs broken down by this route increases the bioavailability of these drugs and the result is a significantly elevated blood concentration of drugs that are substrates of CYP3A4. These medicines include erythromycin, diazepam, alprazolam, verapamil, loratadine, hydrocortisone, sertraline, dextromethorphan, indinavir, caffeine, and paracetamol.[21-26]

By definition, the traditional herbal medicinal products are those herbal medicinal products that have been used for at least 30 years, including at least 15 years within the EU and are intended to be used without the supervision of a medical practitioner and are not administered by injection. [26-30] Some examples of herbals used in traditional herbal medicinal products are: Calendula officinalis L.; Echinacea purpurea L., Moench; Eleutherococcus senticosus (Rupr. et Maxim.) Maxi; Foeniculum vulgare Miller subsp. vulgare var. vulgare; Foeniculum vulgare Miller subsp. vulgare var. dulce (Miller) Thellung; Hamamelis virginiana L; Mentha x piperita L. and Pimpinella anisum L.[26-30]

It is possible for herb-drug interactions to enhance treatment by improving drug bioavailability but harmful herb-drug interactions are understandably a higher priority in terms of public health. An herbal product will be considered a medicinal product when presented as having properties for treating or preventing disease in human beings or where it has a pharmacological, immunological or metabolic action. [31-33]

It is known that the anticoagulant warfarin is the most common drug involved in interactions with the herb St John wort. The concomitant use of St John's wort (*Hypercium perforaum*) with immunosuppressives (e.g. ciclosporin), antiretrovirals (e.g. indinavir), cardiac (e.g. digoxin) or antineoplastic (e.g. irinotecan) drugs may result in reduced plasma concentration of the drug and reduced efficacy by various mechanisms. Ginko biloba has been reported to cause spontaneous bleeding and may produce an additive effect with anticoagulants and antiplatelet agents. Herbal medicine may also interact with each other and many herb combinations. Herbal products may also be taken to enhance the effect of conventional drugs and reduce side effects showing the potential for beneficial herb-drug interaction. [34-36]

Pharmacodynamic interactions involve:
- receptor binding
- post-receptor effects
- systematic or organ effects
- chemical interactions

Interactions can sometimes be predicted on the basis of their pharmacology and chemistry. Pharmacokinetic interactions occur when drug Absorption Distribution Metabolism or Execretion (ADME) processes are altered by another drug and these are the most common types of mechanism (Figure 1).

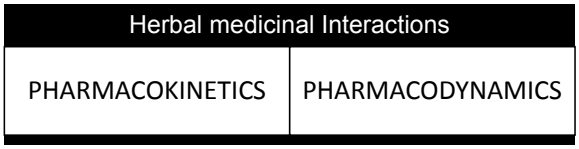

Figure 1. The main interaction classifications of herbal drugs

Table 1 illustrates the interactions activity between some drugs and herbal medicinal products.

Table 1. Some examples of documented interactions of herbs that may be taken in self- medication

Herbal Drug	Prescribed Drug	Interactions
Cranberry[5]	Warfarin	Increased plasma level of warfarin
Ginkgo biloba[8,9]	Tolbutamide	Decreased tolbutamide blood concentrations
Ginseng[10]	Phenelzine	Sleeplessness
Hibiscus[13]	Paracetamol	Changes in paracetamol pharmacokinetics
St John wort [15,16]	Alprazolam, amitriptyline, bupropion, imatinib	Decreased blood concentrations

Glycoprotein is a multidrug resistance protein that transport many important drugs. Glycoprotein is regulates drug bioavailability. In the intestinal epithelium, it pumps drugs back into the lumen; in the liver it excretes them into bile ducts; in the kidney it excretes them into the urine; and in the blood brain barrier it pumps them back into the capillaries.[27-30]

Conclusion

Herbal medicines are widely used by older adults and children and both groups have different rates of me-

tabolism. Older patients in addition to having a generally slower metabolism may take herbal medicines for degenerative conditions and are also more likely to be taking multiple medications. The use of herbal and nutritional supplements is increasing and the practice of integrated medicine is becoming more acceptable. This mean that the pharmacist and other health professionals may be asked by patients about the advantages (if any) of talking certain herbal medicines.

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