Running head: prx and drug to drug interactions

The PXR has been used in various drug to drug interaction techniques as a measure that has ushered in radical medical breakthroughs that promise to elongate human longevity, and at the same time, improve the quality of human life. This paper therefore seeks to explain the types of the PXR drug to drug transactions, and the advantages that have been accrued, and how the procedures have been administered. The prospects of drug to drug interaction has been a matter under close scrutinization to the researchers, consumers, clinicians and the medical fraternity at large.

The drug to drug interactions also include the herbs and drugs interaction that has recently sparked a lot of unprecedented interest among researchers who are now coming to accept the potentiality of herbs in the field of medicine and research. Most of the interest in the herb and drug interaction is being focused on by the St. John's wort. This section is working on a herbal cure for depression which is normally known to have some repercussions on the metabolism of diverse drugs.

These groups of drugs comprise drugs used to cure or control asthma, depression disorders, immune system disorders, and high blood pressure. Within this rubric also falls the birth control pills (Sies and Packer, 2003 pp. 56). The prospects of the significance that would stem from the herbs and drugs interaction has been bolstered by the research that was carried out by Dr. Kliewer. The research was done on the nuclear receptors which are types of proteins that are known to trigger specific body functions, and also shown to have a clear nexus between metabolism and diseases. Dr.

Kiewer's study was focused on a PXR as a variant of the nuclear receptors, for exotic substances that are known as the Xenobiotics. This expedition led

to more discoveries on the interactions between the herb and drugs (Lee, Obach and Fisher, 2003 pp. 110). Upon being triggered, the PXR initiates spates of reactions that are aimed towards exterminating substances that are known to be potentially dangerous to the body. Dr. Kleiwer divulges that unlike other nuclear receptors which are normally triggered by only certain substances, the PXR can be set off by divers and sundry chemical substances.

This gives the PXR an edge over its nuclear receptor counterparts, thus making it the most ideal nuclear receptor to be used for the protection from divers chemical invasions (Rodriguez, 2002 pp. 177)). However, it was also found that certain drugs and herbs falling within the category of the St. John's wort had the ability to trigger the PXR, and thereby, catalyzing the body's metabolism. This culminates into the body being susceptible to hazardous drug level. Through subsequent researches, Dr. Kleiwer and his team was able to ascertain the substance that set off the PXR.

This led to the conclusion that herbs were interactable with drugs. It is on this backdrop that herbs were found having the capacity to treat obesity and high cholesterol upon being tinkered with using other drugs. An example of this is the guggulipid, a traditional herb from India. In the same wavelength, a herb also known to have the ability to set off the PXR, the hops, has been known to be the curative for anxiety, insomnia and indigestion (Di Guilio and Hinton, 2008 pp. 245)). More breakthroughs are likely to be realized, since the medical fraternity, through Dr.

Kliewer's researches is now able to predict and to avoid these kinds of drug interactions. Another example of drug to drug interaction that involves the

PXR's use is in the field of anticancer drug to drug interaction (Paumgartner, 2005, pp. 133). This also involves the use of the clinically relevant drugs and the St. John's wort. This is because the latter is known to bring in a cooling effect on cancer patients during attacks from depression (Goffin and Kelly, 2007 pp. 120). This came after it was found out that the cancer patients who used a mixture of Irinotecan and the St.

John's wort had 42%lower cases of attacks by depression (Rang, 2006 pp. 99). The same state of development was exhibited by mice that were exposed to St. John's wort for 14 days. This, among the mice led to abated cases of the SN- 38 and the Irinotecan concentrations. In the absence of the St. John's wort, among the cancer patients, cases of myelosuppression soared. Among the mice, hematological and gastrointestinal toxins were also seen to have risen in the absence of the St. John's wort. However, this method has been in use until when further researches found out that the St.

John's wort seemed to be having a reducing effect on the level of plasma. The PXR has also been used to detoxify the body since it is also known to have a reducing effect on the Xenobiotics. This followed the development of the discovery whereby, orphan nuclear receptors responsible for the triggering of the metabolic enzymes, and the transporters of the ABC drugs, were identified. For this, there were: the PXR as the X pregnane receptor, the CAR as the receptor to the constitutive androstane, and the receptor to the vitamin D- binder, the VDR.

At the setting off of both the exogenous and the endogenous ligands, the receptors made the heterodimers. These heterodimers mix with the retinoic acid to contain the Xenobiotic elements that respond in the target genes

(Doherty, 2003 pp. 187). This process leads to the increased transcoding of the target genes, a development that leads to the reduction of the Xenobiotic elements and consequent detoxification. The PXR has also been used as a mechanism to induce the absorption and the transportation of other drugs.

This is due to the fact that (SRX) xenobiotic receptor which is also a variant of the PXR, has been known to recently function as the chief transcriptional regulator of the PGP and the CYP3A4. In addition to the above, other enzymes that catalyze metabolism (these include the Sulfotransferace, and the glutathion sulfotransferace), were also found to be under the control of the PXR (Cseke, 2005 pp. 520). The human PXR ligands are also known to be the inducers of certain drugs such as Clortrimazole, Paclitaxel, Dexamethasone, and the Rifampiucin, among others. Further research also revealed that the St.

John's worm's capacity is also supported by the PXR. For instance, the St. John's wort which is known as a strong component of the hyperforin, is activated by the PXR to induce CYP2C9. The same hperforin forms a compound of the human PXR, in the ligand- binding domain. This indicates that the activities of the PXR among myriads of mechanisms, facilitates the induction of the enzyme metabolism. Thus, It is on this backdrop that the use of the PXR has been used in the medical and the pharmaceutical fraternity since the PXR possesses a high ability to heighten the absorption of clinically significant drugs (Trauner and Jansen, 2004 pp. 39).

In addition to this, PXRs portray the ability to facilitate the transportation of chemotherapeutic drugs. This leads to the increased therapeutic efficiency

and the lessened toxicity of drugs. This has led to rising up of effective methodology of analyzing the in vitro and in vivo modes of administering drugs and heath care through the use of PXR's inductive role and capacity. A research was also carried out in Australia (Boullata and Armenti, 2004 pp. 201), in which nuclear receptors PXR, together with its close affiliates, the RXRQ, and the HNF4Q, had molecular studies carried on them.

The domains of the PRX proteins were first and foremost (in importance)identified so as to support the interaction with the rest of the molecules found in the liver cells. This is after the setting off of the PXR through the use of other drugs. The interactions with the co factors of other proteins which drive the PXR into the nucleus is noted. This process leads to the formation of a dynamic multi- protein compounds which are needed to trigger the target genes.

The PXR, the RXR, and the HNF4 protein variants such as phosphorylation come in to modulate the interactions with other proteins. This technique has been very beneficent in the field of medical and health sciences, and in the prolonging of the longevity of human life. This is so because, diseases like cancer which have inflammatory elements, are able to have their activities which disintegrates the human cells altered, through the use of the nuclear receptors to change their state of phosphorylation (Krishna, 2004 pp. 03). It is through this process that the role of the PXR in shielding human cells from radioactive rays on radiotherapy being carried out, has been discovered. Radiotherapy leads to the destruction of the quickly dividing cancer cells' genetic component, which is good, but nevertheless, a problem also sets in,

since radiotherapy also depletes most components of both conventional and the destructive cancer cells.

Cholesterol that have been attached to the membranes can also be altered by the diverse forms of radiation, and thus, can prove highly toxic to the cells. However, the PXR has been transformed with the eons of time, to shield cells from the dangerous molecules that have been created in an endogenous sense. It is also because of this same fact that the PXR also has the capacity to extirpate foreign chemicals and to plummet their activities which cause the wasting away of normal cells (Kaplowitz and De Leve, 2003 pp. 5). To this effect, the contribution of the PXR in the triggering of the pathways of detoxification has been, and is still being extensively researched on. This has consequently lessened the use of radiotherapy which normally causes collateral damage to the cells' components. With more research on the PRX, and use of the PXR, ameliorations are likely to emerge, probably leading to the shelving away of radiotherapy as a way of treating cancer.