Teratogenic and Neuro-Developmental Screening of Some Commonly used Medicinal Plants in Nigeria.

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Introduction:

Herbal medicines play significant roles in the management of both minor and major illnesses (Eisenberg et al., 1993; Barnes, 2003; Gardiner et al., 2007), and their use has been on increase in many developing and industrialized countries (Ernst, 2003). And about 65%-80% of the world's population use traditional medicine as their primary form of health care (World Health Organization, 2007).

This increase in the use of herbal medicine has been influenced by patients' dissatisfaction with conventional allopathic medicines in terms of effectiveness and/or safety (Abbot, 1997) and the perception that herbal medicines are inherently safe because they are natural.

However, despite the profound therapeutic advantages possessed by some of these medicinal plants, some constituents of medicinal plants have been shown to be potentially toxic, mutagenic, carcinogenic and teratogenic (Gadono et al., 2006).

If some medicinal plants can be potentially toxic, then, there is the need to evaluate the teratogenic potentials of some of the plants commonly used by pregnant women in Lagos Nigeria.

Hence, we evaluated the teratogenic potentials of three medicinal plants that were carefully selected following an ethnobotanical survey of plants commonly used in pregnancy.

Experimental design:

1. Plants were extracted by maceration
2. The plants were screened for incidence of early life stage toxicity using zebrafish embryos.
3. The plants were accessed for their teratologic effect on the developing blood using transgenic *Tg(gata1:dsRed)sd2/+(AB)* zebrafish embryos at 72 hours post fertilization (hpf).
4. The effect on the development of the endothelial vessels were also evaluated using transgenic *Tg(Fli-1a:nEGFP)^{y7}/+(AB)* zebrafish embryos at 72 (hpf).
5. The neurodevelopmental and behavioural effect was accessed by: accessing the disruption of the motor neurons in 72 hours post fertilization zebrafish, and looking for the effect on locomotion in 6 days post fertilization and adult zebrafish.
6. Also, the expression of the genes responsible for the development of the blood and endothelial vessel was evaluated.

Summary of findings:

1. One of the plants showed no morphologic developmental toxicity to Zebrafish embryos. However, another showed a dose dependent gross delay in development which eventually lead to embryo lethality.
2. The last plant screened showed a dose dependent effect on the developmental process which include: skeletal dysmorphogenesis, pericardial edema which led to the formation of a tubular heart and minor lethality of the embryos.
3. There was a dose dependent decrease in the relative velocity of the blood cells which is an indication of a reduced flow rate.
4. A dose dependent decrease in circulating blood was observed. However, the total number of blood cells was not affected and
5. Also, there was a dose dependent disruption in the developing vasculature of the Zebrafish especially affecting the inter-segmental vessels.
6. Although there was a change in the arrangement pattern of the motor neurons, it produced no significant change in locomotion assay carried out in both larva and adult Zebrafish.
7. There was a dose dependent change in the expression of the genes regulating angiogenesis.

Conclusion:

Though medicinal plants have been found to be very useful in the treatment of various ailments we have been able to show that they can also be teratogenic by the study using Zebrafish. Hence, there should be an increased awareness as to the risk posed by these plants to the unborn child.

Summary of Techniques Learnt

The setting up and use of various strains of Zebrafish in toxicological and teratologic research: Which I am planning (as soon as I get the funds) to set up (with the support of the Carvan Lab) the first Zebrafish facility in my institution and possibly the first of its kind in my country for toxicological and most especially teratological screening.

I have become proficient with the use of Zebrafish for behavioral research using the Noldus Danio vision box and analysis using Ethovision software.

Also, I learnt how to do genetic studies (i.e. DNA and RNA isolation, genotyping, PCR techniques using ultramodern equipment).

Furthermore, I acquired some imaging techniques using the fluorescent steromicroscope, High powered fluorescent confocal microscope acquiring 3D images and videos.

I also, had the opportunity to visit the DOW Chemical company in Michigan where I was taught (under the supervision of Dr. Edward Carney a friend of Dr. Carvan) how to perform the Whole Embryo Culture using rat embryos. My *in-vivo* rodent teratologic screening skills were further refined and sharpened at DOW.

Some of the findings of this research were presented by way of poster presentation with the abstract no. 804 titled, "Elucidation of the mechanisms of Teratogenicity of some commonly used Medicinal plants" at the 53rd Society for Toxicology (SOT) annual meeting held in Phoenix, Arizona, USA, March 23-27 2014.

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