https://dx.doi.org/10.4314/dujopas.v10i4a.22
ISSN (Print): 2476-8316
ISSN (Online): 2635-3490
Dutse Journal of Pure and Applied Sciences (DUJOPAS), *Vol. 10 No. 4a December 2024*

The Effect of Jatropha Tanjorensis Leaf Extract on the Histology of the Spinal Cord of Albino Rat Fetuses

[1]*Apochi Obed Okwoli, [1]Mokutima Amarachi Eluwa, [2]Mshelia Philemon Paul, [3]Priyaranjan Maral

[1]Department of Anatomical Sciences
University of Calabar,
Calabar, Nigeria.

[2]Department of Physiology
Abubakar Tafawa Balewa University,
Bauchi, Nigeria.

[3]School of Behavioural Forensic
National Forensic Sciences University,
Gandhinagar, Gujarat, India.

Email: apochiobed@gmail.com

Abstract
Jatropha tanjorensis J.L.Ellis & Saroj is a medicinal plant used in traditional medicine across Africa, Asia, and Latin America to treat various ailments. However, the safety profile of its use during pregnancy is inadequate. The aim of this study was to assess the effect of Jatropha tanjorensis leaf extract on the histology of the spinal cord of albino rat fetus. Fifteen pregnant albino Wistar rats were divided into 3 groups: Group A (control) received normal feed, Group B received 1000 mg/kg of the aqueous leaf extract, and Group C received 1500 mg/kg of the extract. The extract was administered on days 7-11 of gestation. On day 20, the rats were sacrificed and the foetal spinal cords were examined histologically. The control group showed normal spinal cord architecture. Group B fetus showed a moderately enlarged central canal occluded with blood, smaller myelin sheath, and sparse nerve fibers. Group C fetus exhibited a remarkably enlarged central canal, well-stained intermediate zone nuclei, smaller myelin sheath, and sparse marginal zone nerve fibers. The results suggested that the aqueous extract of Jatropha tanjorensis has teratogenic effects on the developing spinal cord of rat fetus, with more pronounced effects at the higher dose. This indicates the extract can cross the placental barrier and negatively impact foetal spinal cord development.

Keywords: Adverse reactions, Herbal remedies, *Jatropha tanjorensis*, Pregnancy, Spinal cord

INTRODUCTION
The widespread use of herbal remedies during pregnancy raises concerns about their safety. Scientific literature highlights the potential adverse effects of herbal products on foetal development, emphasizing the need for thorough investigation. Traditional herbal treatments, while perceived as safe, can pose risks, including rare cases of severe consequences. (Vanherweghem & Degaute, 1998; Svedlund *et al.,* 2017; Ernst, 2002; Hu *et al.*, 2023).

Author for Correspondence

Jatropha tanjorensis (Ellis & Saroj, 1961) is a medicinal plant that has been used in traditional medicine across Africa, Asia, and Latin America to treat various ailments and is consumed as a leafy vegetable and also used as a medicinal plant in Nigeria (Irinmwinuwa *et al.,* 2023). It has been reported to have hematological, antimalarial, antibacterial, hypoglycemic, hypolipidemic, and antihypertensive properties (Falodun *et al.,* 2013; Amaechi *et al.,* 2022).

More than 400,000 tropical flowering plant species are known to have therapeutic qualities, which makes traditional medicine far less expensive than modern medicine (Aibinu *et al.,* 2004). In this regard, more than 110,000 publications have been made between 1960 and 2019 alone (Salmerón-Manzano *et al.,* 2020). Since it is thought to be quite safe and free of side effects. Consequently, the rate of patronage has increased over time. While traditional medicines are safe when used as directed by a physician and with very rare cases of potentially fatal consequences. (Adams, 2011; Hartka & Hewitt 2024). Herb used during pregnancy should be done very carefully to avoid harming the fetus or having a negative effect that could result in miscarriage or birth defects (Bercaw *et al.,* 2010; Balarastaghi *et al.,* 2022).

Expectant mothers are using herbal items more frequently even though there is insufficient information to support their usage during pregnancy. Between 7% and 55% of pregnant women use herbal medication, depending on their ethnicity, location, ~~and~~ social and cultural context, Because herbal medications are commonly used during pregnancy, control of these medications is necessary to guarantee their safety and ascertain the contents and effectiveness of the preparations. In the research, friends and family were frequently used as information and referral sources (Dugoua, 2010).

Alternative medicine is widely used in the general population, with recommendations made by people based on their personal experiences as well as that of others around them. (Holst and others, 2008).

Pregnancy causes significant physiological changes, which can lead to a variety of pregnancy-related issues, such as heartburn, nausea, vomiting, and constipation (Lindzon *et al.,* 2011). Pregnant women who experience these ailments typically turn to over-the-counter (OTC) pharmaceuticals, prescription drugs, or herbal remedies as a form of self-medication (Wells, 2009). However, even among these options, people favor herbal products over pharmaceutical drugs because they think they're safer for the developing foetus than contemporary treatment. However, given that the target organ of toxicity in herb use is not always the site of accumulation, herbs may be much more problematic (Curtis, 2001), they might have unanticipated negative effects on the mother and fetus. (Bercaw and others, 2010).

Kodali & Segal (2024) states that drugs will enter the baby's system through the placenta after the fertilized egg implants in the womb and, if taken adversely, may impair the development of the foetus. Also, it was discovered that medications used within the first week following fertilization typically have an "all-or-nothing" effect; that is, they can have no negative effects, but when they do, the embryo is typically lost (Consumer Reports, 2014). This suggests that a drug's or herb's potential for damage varies depending on the stage of pregnancy. For instance, the first trimester (2 – 8 weeks), when the primary organs and body components grow, is typically when the most serious birth abnormalities occur, and sadly, babies are at greater risk of having a neural tube birth defect (Alwan *et al.,* 2007).

Neural tube defects (NTDs) impair about 4000 births and pregnancies annually in the United States, or 1.1 births per 1000 births on average (Avagliano *et al.,* 2019). A birth condition known

as a neural tube defect is characterized by the deformity of bodily parts connected to the brain and spinal cord. The central nervous system's organizer and predecessor, the neural tube, is where an NTD begins and is identified by its inadequate closure. Anencephaly (a lack of brain and skull), hydranencephaly (cerebral hemispheres replaced with sacs of cerebrospinal fluid), spina bifida occulta (incompletely closed lower spinal cord), iniencephaly (severe retroflexed head and spinal defects), and encephalocele (a saclike protrusion from an opening somewhere along the midline of the skull) are among the anatomical abnormalities in humans caused by incomplete neural tube closure during embryonic development (Cooper-Roth, 2010).

Both DNA and RNA are biosynthesised with the help of methylation processes and nucleic acid synthesis. NTDs are caused by a deficiency in folic acid or a lack of the enzymes needed to metabolize folic acid into folate. This is because early pregnancy is a critical period for the embryo's rapid cell division and growth, which calls for the highest level of DNA synthesis. The neural tube does not shut properly because the embryo is unable to biosynthesize DNA at an efficient pace and so cannot produce the required proteins. (Cooper-Roth, 2010).

The study aims to explore the effects of *Jatropha tanjorensis* leaf extract on the spinal cord development of albino rat fetus, seeking to bridge traditional knowledge with modern scientific research. The objective is to examine the histopathology of spinal cords in fetus of albino Wister rats to understand the potential pharmacological impacts of the extract. This study's outcome will help determine if the use of *Jatropha tanjorensis* aqueous extract should be promoted or discouraged based on its potential teratogenic effects.

This study involves light-microscopy histological observation to assess how *Jatropha tanjorensis* (Hospital too far) affects the spinal cord development in albino Wister rat fetus. If no negative impact is found, its moderate use could be encouraged, but if teratogenic effects are observed, its use could be discouraged.

MATERIAL AND METHODS

Breeding of the animal

For this investigation, fifteen mature female albino Wister rats weighing 180–220g were utilized. These were acquired from the animal farm at the University of Calabar. For two weeks, they were housed in the Department of Anatomy's animal house with typical settings of 27°C to 30°C, a 12-hour dark photoperiod, and a 12-hour natural light cycle to help them acclimate. Water was available to the animals at all times, and feed-mash was used for feeding. Following the period of acclimation, they were split into two groups at random: the experimental and control groups. The research was conducted in accordance with the internationally accepted principles for laboratory animal use and care as found in the European Community guidelines (EEC Directive of 1986; 86/609/EEC). The Faculty of Basic Medical Sciences University of Calabar's Faculty Animal Research Ethics Committee (FAREC-FBMS) approved procedures involving the use of animals, with reference number 001C1419.

Extracts Preparation

University of Calabar's Department of Botany verified the authenticity of *Jatropha tanjorensis* leaves that were obtained from the university farm. The plant name has been checked with the "World Flora Online (www.worldflora.org) (WFO, 2024). The voucher specimen (UCAL-3394) was kept in the University of Calabar Herbarium's Department of Botany in Calabar, Cross River State, Nigeria. After thoroughly cleaning the leaves with water to get rid of any contaminants, they were oven-dried for three hours at 45°C to 50°C in a carbolite moisture extraction drying oven (Grent Instrument, Cambridge, England). Using a Binatone household

blender, the dried leaves were ground into a fine powder and stored in glass jars covered with plastic. One liter of purified water and a known weight of the blended sample were cooked for ten minutes at 50°C. After heating the mixture, it was filtered and vacuum-evaporated. Brown and viscous, almost pasty fluid was the end result.

Experimental protocol

The rats' oestrous cycle was monitored by looking at vaginal smears before copulation. For instant mating, those in the oestrous or pre-oestrous phases were divided. These creatures spent the night in a cage with a male rat who was sexually matured. The next morning, the female rats were checked for vaginal plugs, which indicated successful copulation, and the male rats were removed. A vaginal smear was used as a double check, and the presence of spermatozoa verified coitus. Day zero of the pregnancy was identified as the sperm positive day (Singh et al, 1978). The pregnant rats were divided into four groups. Labeled groups A, B and C, each consisting of 5 rats. The aqueous extract of *Jatropha tanjorensis* leaf was administered orally with the aid of orogastric tube to the animals in the experimental groups on days 7^{th} – 11^{th} of gestation respectively as shown below.

Group A (Control) – Animals were fed with normal commercial feed

Group B – Animals received 1000mg/kg body weight of aqueous leave extract of *Jatropha tanjorensis*.

Group C – Animals received 1500mg/kg body weight of aqueous leave extract of *Jatropha tanjorensis*.

On the 20^{st} day of gestation, the rats were sacrificed by chloroform anaesthesia. Fetus were harvested by uterectomy, blotted dry with filter paper and the spinal cord were the excised and fixed in 5% formaldehyde for histological study.

Following sacrifice, the fetus' spinal cords were stored in 5% formaldehyde for 48 hours. Thereafter, the cords were subjected to two changes of increasing alcohol grades (70, 90%, 95%, and 100%) for an hour each in order to dry them. It was then cleared in two xylene changes (xylene I and II) for one hour at a time. Following that, it was embedded in three paraffin wax changes for thirty minutes apiece in an impregnation oven set at 57°C. After that, it was mounted on wooden blocks and blocked using the Leuckhart metal mould/block in the shape of an L. Thin portions were removed at 5 microns using a rotatory micrometer. And then spent five minutes staining with hematoxylin. After separating sections with 1% acid alcohol and counterstaining them with 1% eosin, excess hemoglobin was removed using water. After being dehydrated with alcohol at 70%, 90%, and 100%, the tissue was cleaned in xylene to eliminate any remaining water. A 22 by 22mm cover slip was placed over a drop of mountant that had been applied to the slides' surface.

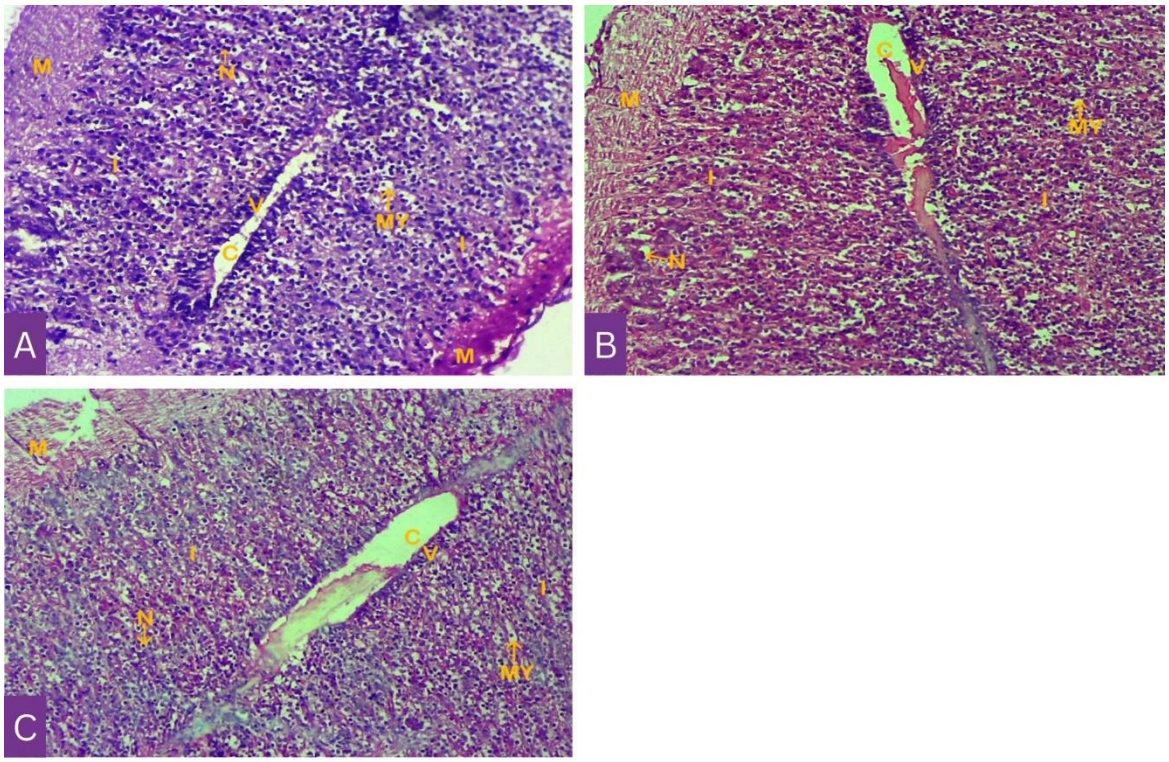
RESULTS

Histological Observations

Histological study of the sections of foetal spinal cord using Heamatoxylin and Eosin staining method showed in the control group A normal cytoarchitecture of the three zones, marginal, intermediate and ventricular with normal central canal. The nuclei of the neurons and myelin sheath in the intermediate zone are well stained. The nerve fibers in the marginal zone appeared thick.

In group B animals whose mothers received 1000mg/kg body weight of aqueous leave extract of *Jatropha tanjorensis* from 7th to 11th days of gestation, the sections of spinal cord of the fetus shows moderate enlargement of the spinal cord with blood occlusion. The nuclei of the neurons in the intermediate zone are well stained. The myelin sheath appears smaller. The nerve fibers in the marginal zone appear sparse when compared with the control.
In group C animals whose mothers received 1500mg/kg of aqueous leave extract of *Jatropha tanjorensis*, the section of spinal cord of the fetus shows remarkably enlarged central canal with blood occlusion when compared with the control and group B sections. The nuclei of the neurons in the intermediate zone are well stained. The myelin sheath appears smaller. The nerve fibers in the marginal zone appear sparse.

Photomicrographs



***A:** Control Group; **B:** 1000mg/kg of aqueous JT and **C:** 1500mg/kg of aqueous JT*

Group A (Control) - Spinal cord showing normal architecture of the three zones, marginal (M), intermediate (I) and ventricular (V). The central canal (C) appears normal. The nuclei (N) of the neurons and myelin sheath (MY) in the intermediate zone are well stained. The nerve fibers in the marginal zone appear thick. (H & E. x100).

Group B – 1000mg/kg of aqueous extract of *Jatropha tanjorensis* showing the architecture of the three zones, marginal (M), intermediate (I) and ventricular (V), with moderately enlarged central canal (C) occluded with blood. The nuclei (N) of the neurons in the intermediate zone are well stained. The myelin sheath (MY) appears smaller. The nerve fibers in the marginal zone appear sparse (H & E. x100).

Group C – 1500mg/kg of aqueous extract of *Jatropha tanjorensis* showing the architecture of the three zones, marginal (M), intermediate (I) and ventricular (V). The central canal (C) is remarkably enlarged and occluded with blood. The nuclei (N) of the neurons in the

intermediate zone are well stained. The myelin sheath (MY) appears smaller. The nerve fibers in the marginal zone appear sparse (H & E. x100).

Histological analysis revealed distinct changes in the spinal cord architecture of rat fetus exposed to the *Jatropha tanjorensis* extract. Group B showed a moderately enlarged central canal with blood occlusion, while Group C exhibited a remarkably enlarged central canal, altered myelin sheath, and sparse nerve fibers. These findings suggest a significant impact of the extract on foetal spinal cord development.

Discussion

The study plant, *Jatropha tanjorensis*, is used in traditional medicine throughout Africa, Asia, and Latin America to treat a variety of illnesses (Burkill, 1994). This is due to a variety of factors, including its antioxidant properties (Gilbert, 2017), which can lower the risk of hypertension, as well as its anti-androgenic, hemolytic, antimicrobial, anticancer, anti-inflammatory, diuretic, cancer preventive, hepatoprotective, antibacterial, antitumor, immuneostimulant, chemotherapy, and asthmatic properties (Bharathy & Uthayakumari, 2013). Its regulated hypoglycemic activity makes it helpful in the treatment of diabetes mellitus as well. Gilbert (2017) said.

The results showed moderately enlarged central canal occluded with blood, smaller myelin sheath and sparse nerve fibers in the marginal zone in Group B and C foetus whose mothers received 1000mg/kg and1500mg/kg of the aqueous extract of *Jatropha tanjorensis* but more pronounced in group C as shown in plate A, B and C. This shows that the extract crossed the placental membrane barrier to affect the spinal cord. This is similar to findings by Khedun *et al*. (2000) who reported that extracts can cross the placental barrier and are present in varying concentrations in the foetal circulation, with varying resultant effects on foetal metabolism. Histological studies of the canal indicate that ependymal cell breakdown during the ageing process contributes to the canal occlusion (Cramer, 2005).

The blood in the central canal could be as a result of erosion from the arterioles around the central canal since it is said to contain blood vessels and nerve fibers. Similarly, in findings by Mesembe *et al*. 2004). In his work, the foetal spinal cord whose mothers were treated with artesunate showed the presence of debris in central canal, derangement and alteration of the microarchitecture of the foetal spinal cord. This is in concert with report in literature that teratogenic insults on the developing brain during neurogenic period induces anormalies (Singh *et al.,* 1978; Singh and Padmanabhan, 1978; Igiri *et al.,* 1999).

Cramer (2005) related dilatations of the central canal to syringomyelia. This was first introduced by Ollivier D'Angers in 1827, the term syringomyelia, derived from the Greek word for tube (syrinx), is used to describe dilation of the central canal extending over many segments and appears to be related to a hydrodynamic mechanism related to the cerebrospninal fluid (CSF) (Batzdorf, 1991; Cramer, 2005). In similar studies on kaolin were observed to cause central distention due to the downward movement of CSF from the ventricles in the brain (Becker *et al.,* 1972; Eisenberg *et al.,* 1974; Hall *et al.,* 1975; Hall *et al.,* 1976; Hall *et al.,* 1977; Hall *et al.,* 1980; Williams and Bentley, 1980).

Reduction in nerve fibres was also noticed in relation to Steven *et al.,* (2017). He discovered a reduced intraepidermal nerve fiber density after a sustained increase in insular glutamate: a proof-of-concept study examining the pathogenesis of small pathology in fibromyalgia. In his work, he recognized well reduced peripheral nerve fiber density due to fibromyalgia pathology in relation, the reduced myelin sheath could be as a result of demyelination due to

chemical injury from the extract *J. tanjorensis* or its constituent or dysmyelination which refers to the failure of the myelin to form as in relations to Love, (2006). A diagnosis of demyelination carries important therapeutic and prognostic implications. In most cases the diagnosis is made clinically, and involvement of the histopathologist is largely confined to postmortem confirmation and clinicopathological correlation. However, every now and then, accurate diagnosis of the presence or cause of demyelination before death hinges on the histopathological assessment (Love, 2006).

When myelin is lost but axons are largely preserved, this condition is referred to as demyelination. This is caused by diseases or trauma that harm the cells that make up myelin sheaths or the sheaths themselves (Schäffner *et al.,* 2023). It is important to identify these illnesses from others in which normal myelin formation is disrupted (Staugaitis & Trapp, 2012).

While demyelinated axons may atrophy and eventually degenerate, demyelinating disorders do not include conditions in which myelin deterioration is subsequent to axonal degeneration. According to their pathogenesis, demyelinating diseases of the central nervous system can be divided into several categories, including those brought on by inflammatory processes, viruses, acquired metabolic disturbances, hypoxic-ischaemic forms of demyelination, and focal compression (Höftberger *et al.,* 2002; Love, 2006). There might be increased demyelination. Arterioles and arteries don't usually get inflamed. Axonal fragmentation and minor perivascular hemorrhages could be present. Leptomeninges may include inflammatory cells, and the brain stem and spinal cord may have subpial demyelination (Love, 2006).

Conclusion

In conclusion, this study indicated that the aqueous extract of *Jatropha tanjorensis* has some teratogenic effects on the developing spinal cord of wister rats fetus which aligns with previous research on the teratogenic effects of herbal extracts on foetal development. The observed histological changes indicated potential risks associated with *Jatropha tanjorensis* exposure during pregnancy. The study contributes to understanding the pharmacological actions of traditional herbal remedies and underscores the importance of evidence-based research in evaluating their safety during pregnancy.

Based on the findings it is recommended that the effect of long term consumption of *Jatropha tanjorensis* on the spinal cord should be investigated. Also, studies should be carried out on other organs in the body using advanced research methods such as electron microscope.

REFERENCES

Adams, J. (2011). Growing popularity of complementary and alternative medicines during pregnancy and implications for healthcare providers. *Exp. Rev. Obstet. Gynecol*., **6**(4): 365-366.

Aibinu, I., Adenipekun, T., Adelowotan, T., Ogunsanya, T. & Odugbemi, T. (2004). Evaluation of the antimicrobial properties of different parts of *Citrus aurantifolia* (lime fruit) as used locally. *Afr. J. Tradit. Complement. Altern. Med*., **4**(2): 185-190.

Alwan, N. A., Hamamy, H. & Al-Haddad, S. (2007). Neural tube defects and folic acid fortification in the new millennium. *Genet. Med*., **9**(12): 818-831.

Amaechi, D., Yisa, B. N., Ekpe, I. P., Nwawuba, P. I., & Rabbi, A. (2022). Phytochemical screening, anti-obesity and hepatoprotective activities of ethanol leaf extract of *Jatropha tanjorensis* in Wistar rats. *Asian J. Appl. Chem. Res*, 12(4), 20-26.

Avagliano, L., Massa, V., George, T. M., Qureshy, S., Bulfamante, G. P., & Finnell, R. H. (2019). Overview on neural tube defects: from development to physical characteristics. *Birth Defects Res*., 111(19), 1455-1467.

Balarastaghi, S., Soleimani, M., Soleimani, A., Soleimani, M., & Soleimani, A. (2022). Herbal medicine uses during pregnancy: a systematic review and meta-analysis. *J. Matern. Foetal Neonatal Med.*, 35(12), 2305-2315.

Batzdorf, U. (1991). Syringomyelia: current concepts in diagnosis and treatment. *Neurosurg. Clin. N. Am*., 2(4), 633-641.

Becker, D. P., Wilson, J. A., & Watson, G. W. (1972). The spinal cord central canal: an experimental study of pressure response to experimental alterations of cord volume, pressure, and compliance. *J. Neurosurg.*, 36(6), 724-734.

Bercaw J, Maheshwari B, Sangi-Haghpeykar H. (2010). The use during pregnancy of prescription, over-the-counter, and alternative medications among Hispanic women. *Birth*. 37 (3):211-218.

Bharathy V and Uthayakumari F., (2013). Bioactive Components in leaves of Jastropha *tanjorensis* J.L. Ellis & Saroja by GC-MS Analysis. *Int. J. Pharm. Sci. Res*. Vol. 5, No.4, pp 1839-1843, 2013.

Burkill, H. M. (1994). The useful plants of West Tropical Africa. Vol. 2: *Families EI* (No. Ed. 2, pp. xii+-636).

Consumer Reports. (2014, July). Health risks of taking drugs during pregnancy. *Consumer Reports*. https://www.consumerreports.org/cro/2014/07/drugs-you-take-while-pregnant-may-not-be-as-safe-as-you-think/index.htm

Cooper-Roth, T. (2010). Neural tube defects (NTD): Folic acid and pregnancy. *Embryo Project Encyclopedia*. http://embryo.asu.edu/handle/10776/2295

Cramer, G. C. (2005). General anatomy of the spinal cord. In G. D. Cramer & S. A. Darby (Eds.), Basic and clinical anatomy of the spine, spinal cord, and ANS (pp. 122-124). *Elsevier Mosby*.

Curtis, D. K. (2001). Principles of toxicology. In J. G. Hardman & L. E. Limbird (Eds.), Goodman and Gilman's the pharmacological basis of therapeutics (10th ed.). McGraw-Hill.

Dugoua, J. J. (2010). Herbal medicines and pregnancy. *J. Popul. Ther. Clin. Pharmacol*., 17(3), e370-e378.

Eisenberg, H. M., McLennan, J. E., & Welch, K. (1974). Ventricular perfusion in cats with kaolin-induced hydrocephalus. *J. Neurosurg.*, 41, 20-28.

Ellis, J. L., & Saroja, T. L. (1961). A new species of Jatropha from South India. *Journal of the Bombay Natural History Society*, 58, 834-836.

Ernst, E. (2002). Toxic heavy metals and undeclared drugs in Asian herbal medicines. *Trends Pharmacol. Sci.*, 23, 136-139.

Falodun, A., Udu-Cosi, A. A., Erharuyi, O., Imieje, V., Falodun, J. E., & Agbonlahor, O. (2013). *Jatropha tanjorensis*: Review of phytochemistry, pharmacology, and pharmacotherapy. *J. Pharm. Allied Sci*., 10(3), ISSN: 1596-8499.

Gilbert, E. (2017). *Jatropha tanjorensis* ("Hospital too far", Ugu-Oyibo, Iyana-Ipaja); an underutilized medicinal plant. *Health Bubbles*. http://healthbubbles.com/gb/?p=3534

Hall, P., Turner, M., & Aichinger, S. (1980). Experimental syringomyelia: The relationship between intraventricular and intrasyrinx pressures. *J. Neurosurg*., 52, 812-817.

Hall, P. V., Kalsbeck, J. E., & Wellman, H. N. (1976). Radioisotope evaluation of experimental hydrosyringomyelia. *J. Neurosurg*., 45, 181-187. https://doi.org/10.3171/jns.1976.45.2.0181

Hall, P. V., Lindseth, R. E., Turner, M. L., Campbell, R. L., & Mealey, J. Jr. (1983). Alterations in cerebrospinal fluid dynamics in syringomyelia, hydromyelia, and

myelomeningocele. Neurobiol. Cerebrospinal Fluid. Wood JH (Ed): *Plenum Press,* NY, 895-911. https://doi.org/10.1007/978-1-4615-92693_57

Hall, P. V., Muller, J., & Campbell, R. L. (1975). Experimental hydrosyringomyelia, ischemic myelopathy, and syringomyelia. *J. Neurosurg*., 43, 464-470. https://doi.org/10.3171/jns.1975.43.4.0464

Hall, P., Godersky, J., & Muller, J. (1977). A study of experimental syringomyelia by scanning electron microscopy. *J. Neurosurg*., 1, 41-47. https://doi.org/10.1227/00006123-197707000-00009

Hartka, T., & Hewitt, M. A. (2024). Prediction chapter of medical need and event risk assessment at mass gathering events. In Mass Gathering Medicine: A Guide to the Medical Management of Large Events (p. 21).

Höftberger, R., Guo, Y., Flanagan, E. P., Lopez-Chiriboga, A. S., Endmayr, V., Hochmeister, S. ... & Lucchinetti, C. F. (2020). The pathology of central nervous system inflammatory demyelinating disease accompanying myelin oligodendrocyte glycoprotein autoantibody. *Acta Neuropathol.,* 139, 875-892.

Holst, L., Nordeng, H., & Haavik, S. (2018). Use of herbal drugs during early pregnancy in relation to maternal characteristics and pregnancy outcome. *Pharmacoepidemiol. Drug Saf.*, 17(2), 151-159.

Hu, S., Luo, D., Zhu, Q., Pan, J., Chen, B., Furian, M., & Shi, S. (2023). An updated meta-analysis of Chinese herbal medicine for the prevention of COVID-19 based on Western-Eastern medicine. *Front. Pharmacol*., 14, 1257345. https://doi.org/10.3389/fphar.2023.1257345

Irinmwinuwa, E. O., Adolphus, M. C., Opute, R. E., Oyate, G. B., Chinedu, J. O., Afonne, O. J., & Unekwe, P. C. (2023). Review of herbal plant associated with anti-anemic property and mechanism of action. *Int. J. Sci. Res. Arch*., 8(2), 589-601.

Khedun, S. M., Maharal, B., & Moodley, J. (2000). Effects of antihypertensive drugs on the unborn child: what is known, and how should this influence prescribing? *J. Pediatr. Drugs*, 2(6), 419-436.

Kodali, B. S., & Segal, S. (2024). Drug interactions and obstetric anesthesia. In Datta's Obstetric Anesthesia Handbook (pp. 47-70). *Springer International Publishing*.

Lindzon, G., Sadry, S., & Sharp, J. (2011). Obstetric. In Toronto Notes for Medical Students (27th Ed.). *Type & Graphics Inc*., Canada.

Love, S. (2006). Demyelinating diseases. *J. Clin. Pathol*. 59(11), 1151-1159.

Mesembe, O. E., Ivang, A. E., Udoaffah, G., Igiri, A. O., Eluwa, M. A., & Fischer, V. A. (2004). Teratogenic effect of artesunate on the histology of developing spinal cord of Wistar rat foetuses. *J. Biomed. Afr*., 11(1), 92-97.

Salmerón-Manzano, E., Garrido-Cardenas, J. A., & Manzano-Agugliaro, F. (2020). Worldwide research trends on medicinal plants. *Int. J. Environ. Res. Public Health*, 17(10), 3376. https://doi.org/10.3390/ijerph17103376.

Schäffner, E., Bosch-Queralt, M., Edgar, J. M., Lehning, M., Strauß, J., Fleischer, N., ... & Stassart, R. M. (2023). Myelin insulation as a risk factor for axonal degeneration in autoimmune demyelinating disease. *Nat. Neurosci*., 26(7), 1218-1228.

Staugaitis, S. M., & Trapp, B. D. (2012). Diseases involving myelin. In Basic Neurochemistry (pp. 691-704). *Academic Press*. https://doi.org/10.1016/B978-0-12-374947-5.00039-0

Harte, S. E., Clauw, D. J., Hayes, J. M., Feldman, E. L., St Charles, I. C., & Watson, C. J. (2017). Reduced intraepidermal nerve fiber density after a sustained increase in insular glutamate: a proof-of-concept study examining the pathogenesis of small pathology in fibromyalgia. *Pain Rep*., 2(3), e590.

Svedlund, E., Larsson, M., & Hägerkvist, R. (2017). Spontaneously reported adverse reactions for herbal medicinal products and natural remedies in Sweden 2007–15: report from the

Medical Products Agency. *Drugs Real World Outcomes*, 4, 119-125. https://doi.org/10.1007/s40801-017-0104-y

Vanherweghem, J. L., & Degaute, J. P. (1998). The policy of admission to the education in medicine and dentistry in the French-speaking community of Belgium. *Acta Clin. Belg*., 53, 2-3.

Wells, B. G. (2009). Gynecologic and obstetric disorders. In Pharmacotherapy Handbook (7th ed.). *The McGraw-Hill Companies.*

WFO (2024): *Jatropha tanjorensis* J.L.Ellis & Saroja. Published on the Internet;http://www.worldfloraonline.org/taxon/wfo-0000219995. Accessed on: 05 May 2024

Williams, B., & Bentley, J. (1980). Experimental communicating syringomyelia in dogs after cisternal kaolin injection. Part 1. Morphology. *J. Neurol. Sci*., 48, 93-107. https://doi.org/10.1016/0022-510X(80)90153-7