ISSN: 1511-3701
Pertanika J. Trop. Agric. Sci. **34 (2)**: 341 - 349 (2011)

Subchronic Oral Toxicity Study of *Morinda citrifolia* (Mengkudu) in Spraque Dawley Rats

Rosly, S.M.[1]*, Shanmugavelu, S.[1], Murugaiyah, M.[2], Hadijah, H.[3], Ahmad Tarmizi, S.[3], Noridayusni, Y.[1] and Subramaniam, K.[1]

[1]Strategic Livestock Research Centre,
Malaysia Agricultural Research and Development Institute,
MARDI Headquarters
[2]Department of Veterinary Clinical Studies,
Faculty of Veterinary Medicine, Universiti Putra Malaysia,
43400 UPM, Serdang, Selangor, Malaysia
[3]Food Technology Research Centre,
Malaysia Agricultural Research and Development Institute,
MARDI Headquarters, Serdang, G.P.O. Box 12301,
50774 Kuala Lumpur, Malaysia
[*]E-mail: rosly@mardi.gov.my

ABSTRACT

A subchronic oral toxicity study was conducted to evaluate the safety of *Morinda citrifolia* in Sprague-Dawley (SD) rats. For this purpose, the fruit of *Morinda citrifolia* were oven dried and ground into powder form before incorporating into diet and fed to SD rats (10 males and 10 females per group) at dose levels of 2000 (low dose) and 5000 (high dose) mg/kg body weight/day for 13 weeks. Clinical observations were recorded, while body weight and feed consumption were measured throughout the study. At the end of the study, all the rats were subjected to a full necropsy. Their blood samples were collected for clinical pathology, whereas selected organs were weighed and tissues were preserved from all the animals. Total protein was found to be significantly lower ($p<0.05$) in male rats of all the treatment groups. Meanwhile, total white blood cells ($3.96 \times 10^3/\mu l$) and spleen weight (0.14%) were found to be significantly lower ($p<0.05$) in female rats of the low dose group. Nevertheless, the differences observed were within the normal range of normal healthy rats that were considered to be not toxicological significance. It was concluded that the no-observed-adverse-effect level (NOAEL) for *Morinda citrifolia* was 5000 mg/kg body weight/day.

Keywords: *Morinda citrifolia*, oven dried, subchronic, rats, clinical pathology

INTRODUCTION

Morinda citrifolia, which is locally known as "mengkudu", has various names such as "noni" in Hawaii, "Indian mulberry" in Indian subcontinent, "painkiller bush" in the Caribbean and "cheese fruit" in Australia (Nelson, 2001; Ross, 2001; Wang *et al*., 2002). The plant has been used for food and medicinal purposes by Polynesians for more than 2000 years (Chan-Blanco *et al*., 2006). It has also been reported to have assorted therapeutic effects in both human and laboratory animals (Wang *et al*.,

Received: 24 August 2010
Accepted: 23 September 2010
*Corresponding Author

2002). In view of the large number of medical claims that have been made for its efficacy, the most important thing not to be overlooked for *Morinda citrifolia* is the safety aspect of the plant, especially the fruit.

Morinda citrifolia product, such as the juice, is increasingly popular as a functional drink due to the claim indicating its benefits for many illnesses. Since 1996, worldwide production of noni fruit juice has tremendously increased with more than 80 million litres by French Polynesia alone (European Food Safety Authority, 2006). The increase in the consumption of noni fruit juice has brought about the concern over its safety in people who have been drinking the noni fruit juice product. Thus, various toxicological studies have extensively been carried out on the fruit juice (Tahitian Noni) and it has been reported to be safe by Scantox Biologisk Laboratorioum, Lille, Skensved, Denmark March 2000 and May 2001 (West *et al*., 2006); however, there were reported cases of the toxicity, especially liver toxicity. In the period between 2004 and 2006, there were reported cases published whereby the noni fruit juice was suggested to have been responsible for acute hepatitis (Millonig *et al*., 2005; Staldbauer *et al*., 2005; Yüce *et al*., 2006).

Meanwhile, it is important to note that toxicological evaluation is a need in herbal studies. The health promoting benefits of *Morinda citrifolia* have been known for generations and they are extensively used in many countries for its medicinal properties. The increasing use of this plant has resulted in concerns over both the efficacy and safety of the product. Despite the widespread use of *Morinda citrifolia* in Malaysian traditional medicine, a survey of the literature has indicated a lack of proper toxicological evaluation of these local varieties. Due to the high promising and commercial potential of *Morinda citrifolia* products, it is therefore essential that *Morinda citrifolia* be studied for possible toxicity. It is particularly important in detecting toxicity that occurs either after a short period or after a prolonged exposure to *Morinda citrifolia*. Hence, through the toxicity studies in animals, it is anticipated that it can be viewed to safeguard the public health and ensure greater value for money of the herbal product during normal conditions of use. The toxicity studies have also provided a preclinical safety evaluation standard that is expected to be performed before *Morinda citrifolia* can be evaluated in human. The subchronic oral toxicity study of *Morinda citrifolia* was performed in Sprague-Dawley (SD) rats to provide benchmark data so as to understand its safety without the potential confounding variables associated with many commercial *Morinda citrifolia* products. This study was therefore carried out with the objectives to investigate the safety of *Morinda citrifolia* through a 13-week subchronic toxicity study in the male and female Sprague Dawley rats, as well as to determine the no-observe-adverse-effect level (NOAEL) of *Morinda citrifolia* in rats fed at the doses of 2000 mg/kg and 5000 mg/kg body weight.

MATERIALS AND METHODS

Test Material

Fresh fruits of *Morinda citrifolia* were obtained from MARDI Research Station, located in Muadzam Shah, Pahang. The fruit samples were finely sliced into 8 mm in thickness and dried in an oven at 55 - 60 °C for 48 hours. The samples were then ground into powder, followed by incorporating it into commercial rodent diet that had previously been ground before the mixing process. Finally, the combination of dried fruit samples and commercial rodent diets were given as treatment diets for the toxicity trial. The treatment diets were freshly prepared every week according to the body weight of the rats.

Animals Management

Sixty male and female Sprague-Dawley (SD) rats at 6 weeks of age, with an average body weight of 170 - 200 grams, were used in the study. The rats were acclimatized to the housing conditions for a period of 1 week, and the treatment started at the age of 7 weeks. All the rats were individually housed in a polycarbonate

mesh bottom cage during the acclimatization period and, were thereafter kept in a room maintained at a temperature of 25–27°C and a relative humidity of 40–70% with a 12-h light/ dark cycle. Each cage was provided with a colour-coded card containing rat number and for dose level identification.

Experimental Design

The rats were weighed and randomly assigned into three groups (10 males and 10 females per group), namely, control, low dose and high dose according to the randomized complete block design (RCBD). When placed in the study, the average weights of the female and male rats were around 170-190 and 220-240 grams, respectively. The powdered *Morinda citrifolia* fruit were incorporated into the treatment diets at the dose levels of 2000 and 5000 mg/kg body weight/ day for 13 weeks. Meanwhile, the control group received commercial rodent diet only. Feed were given *ad libitum* and all rats had free access to water. The amounts of supplied and residual diet were weighed twice a week (at days 6 and 7) in order to calculate the daily feed consumption. The rats were observed daily for clinical signs and mortality, and were weighed weekly. The animals were let to fast overnight prior to necropsy. At the end of 13 weeks or 91-day test periods, all the rats were euthanatized using overdosed diethyl ether. Upon necropsy, their blood samples were taken via caudal vena cava for clinical pathology (clinical biochemistry and haematology), while selected organs were weighed and specific tissues from all animals were preserved for subsequent histopathology examination. The study was conducted at the Animal House, Malaysia Agricultural Research and Development Institute (MARDI) in Serdang, Malaysia, and was complied with the OECD Guidelines for the Testing of Chemicals (OECD Guidelines 408, 1998).

Clinical Pathology

The serum was analysed for alanine amino tranferase (ALT), aspartate amino transferase (AST), alkaline phosphatase (ALP), gamma glutamyl transferase (GGT), creatinine kinase (CK), urea, creatinine, total protein (TP) and albumin using automated clinical chemistry analyzer (TRX 7010, Biorex Mannheim, Germany). The following haematological components were analyzed: total white blood cells (WBC), red blood cells (RBC), haematocrit/packed cell volume (HCT/PCV), haemoglobin (Hb), mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH), mean corpuscular haemoglobin concentration (MCHC) and platelets, using an automated blood analyzer (Cell Dyn® 3700, Abbott Diagnostic, USA).

Pathology

The main organs, such as liver, kidney, spleen, heart, lungs and testes, were quickly excised for all the excess tissues and immediately weighed after rinsing them in 0.9% cold saline to remove any blood. The organ relative weight (% of body weight) was obtained by dividing the final weight of the organ to the final body weight. The tissue samples of the liver and kidney were routinely processed for histopathology and they were examined under light microscope.

Statistical Analysis

The mean values and standard errors were calculated from the data obtained, and these were then statistically analyzed using SAS version 9.1. Meanwhile, Duncan's multiple range analysis was employed to determine the differences in the parameters of the two sexes and between the treatment groups.

RESULTS

Body Weight

The mean body weights of male and female rats for all the treatment groups are shown in *Figs. 1* and *2*. There was no significant difference observed that was attributed to the administration of the test substance between sexes. There was no difference between the treatment groups in

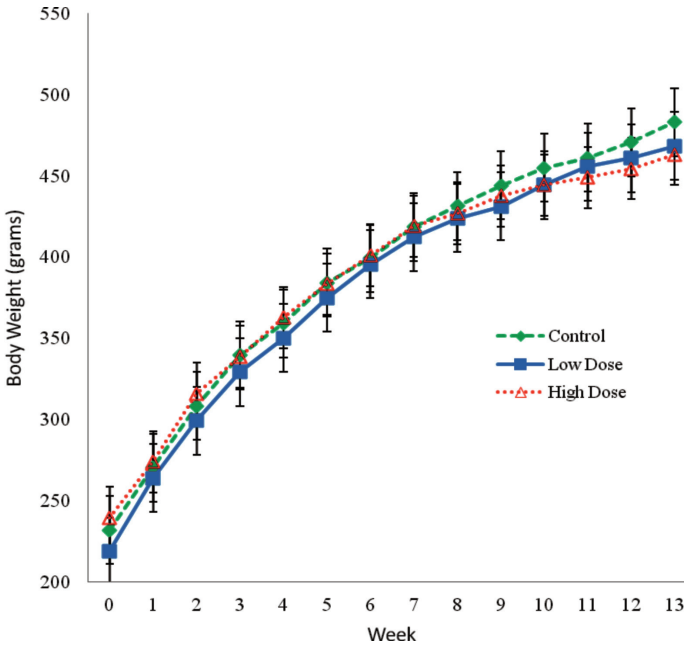

Fig. 1: The mean body weights of the male rats that were given Morinda citrifolia *incorporated in their diet for three months*

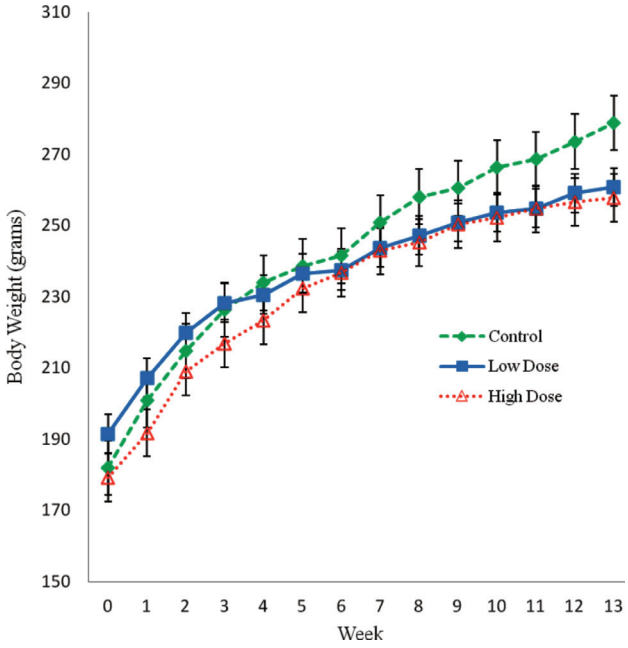

Fig. 2: The mean body weights of the female rats given Morinda citrifolia *incorporated in their diet for three months*

the male rats throughout the experimental period, except at week 2, whereby the body weight was significantly ($p<0.05$) lower in the low dose group (*Fig. 1*). In female rats, the mean body weight was significantly ($p<0.05$) lower at week 12 in the high dose group and in both the low and high dose groups at week 13, as compared to the control (*Fig. 2*).

Clinical Pathology

Generally, there was no significant difference between the sexes in all the parameters measured for haematology (Table 1) and biochemistry (Table 2). Some statistically significant changes between the treatment groups in certain haematology and biochemistry values were also noted. Nevertheless, the magnitudes of the changes were not biologically relevant and the values were also within the normal range of rats of this strain and age. The white blood cells (WBC) count (Table 1) of the females in the low dose group were significantly ($p<0.05$) lower compared to the control and high dose groups. Meanwhile, the total protein (TP) concentration was significantly ($p<0.05$) lower in the male rats as compared to the females in all groups.

Organ Relative Weight

The mean organ relative weights for both the male and female rats in all the treatment groups are shown in Table 3. The spleen weight of the females in the low dose group were significantly ($p<0.05$) lower as compared to the control and high dose groups.

Histopathology

The histopathological examinations of the liver and kidney revealed no significant findings related to the treatments.

TABLE 1
The means haematology values of the treatment groups in the male and female rats
(mean ± S.E.M)

Parameters	Treatment group					
	Control		Low dose		High dose	
	Male	Female	Male	Female	Male	Female
WBC ($\times10^3/\mu l$)	9.78 ± 0.66	5.96[a] ± 0.58	7.95 ± 0.98	3.96[b] ± 0.53	8.78 ± 0.82	4.82[a] ± 0.29
RBC ($\times10^6/\mu l$)	8.85 ± 0.11	7.62 ± 0.17	8.90 ± 0.19	6.92 ± 0.78	8.90 ± 0.11	7.59 ± 0.15
Hb (g/dl)	16.1 ± 0.17	14.4 ± 0.24	16.2 ± 0.34	12.5 ± 1.53	16.1 ± 0.14	14.2 ± 0.27
HCT (%)	50.0 ± 1.24	43.8 ± 1.07	46.9 ± 0.93	37.4 ± 4.23	48.8 ± 1.38	43.4 ± 0.95
MCH (pg)	18.2 ± 0.14	19.0 ± 0.15	18.0 ± 0.10	23.7 ± 6.95	17.9 ± 0.22	18.7 ± 0.15
MCHC (g/dl)	32.4 ± 0.90	33.2 ± 0.72	34.6 ± 0.23	29.9 ± 3.54	33.2 ± 0.86	32.9 ± 0.14
MCV (fl)	56.6 ± 1.56	57.6 ± 1.52	52.1 ± 0.46	48.7 ± 5.55	54.3 ± 1.66	57.4 ± 1.78
PLT ($\times10^3/\mu l$)	1324 ± 25.0	1271 ± 30.9	1298 ± 40.1	1110 ± 42.2	1345 ± 29.8	1350 ± 43.0

[a,b]: Means with different superscript/s within the same row differ significantly ($p< 0.05$)

TABLE 2
The means serum biochemistry values of the treatment groups in the male and female rats (mean ± S.E.M)

Parameters	Treatment					
	Control		Low dose		High dose	
	Male	Female	Male	Female	Male	Female
ALT (U/L)	29.0 ± 0.6	31.2 ± 0.3	26.7 ± 0.5	30.0 ± 0.3	32.7 ± 0.7	31.5 ± 0.4
AST (U/L)	150.7 ± 15.6	149.4 ± 15.0	139.2 ± 11.6	139.2 ± 11.6	132.1 ± 6.2	126.1 ± 11.8
ALP (U/L)	78.6 ± 3.6	63.6 ± 9.7	77.4 ± 4.2	63.4 ± 8.1	89.6 ± 7.1	66.5 ± 9.5
GGT (U/L)	51.3 ± 15.8	23.0 ± 7.2	47.9 ± 11.7	35.0 ± 16.7	67.9 ± 21.0	74.5 ± 4.6
Creatinine (μmol/L)	24.2 ± 15.3	35.9 ± 13.4	16.9 ± 40.2	31.2 ± 12.6	41.5 ± 14.6	40.2 ± 14.2
Urea (mmol/L)	7.5 ± 0.6	6.1 ± 0.5	5.7 ± 0.5	5.8 ± 0.6	6.3 ± 0.8	6.2 ± 0.3
CK (U/L)	197.3 ± 65.1	169.3 ± 61.4	249.0 ± 68.5	177.0 ± 35.1	173.1 ± 51.2	131.6 ± 9.93
TP (g/L)	64.7^{b} ± 1.3	72.9^{a} ± 1.6	65.2^{b} ± 1.2	74.1^{a} ± 1.2	67.9^{b} ± 2.1	74.5^{a} ± 4.6
Albumin (G/L)	40.8 ± 1.2	34.2 ± 0.88	37.3 ± 4.82	34.9 ± 0.43	41.2 ± 2.77	35.9 ± 1.08
Globulin (G/L)	32.0 ± 0.68	30.5 ± 0.92	36.8 ± 4.93	30.0 ± 0.62	33.4 ± 1.88	32.1 ± 1.18
A/G ratio (G/L)	1.3 ± 0.04	1.1 ± 0.04	1.2 ± 0.16	1.2 ± 0.07	1.2 ± 0.02	1.2 ± 0.05

^{a,b}: Means with different superscript/s within the same row differ significantly ($p < 0.05$)

DISCUSSION

In the recent years, there has been growing interest in the safety of herbal products due to a large increase in its consumption as dietary supplements, either for enhancing health or physical performances. The use of complementary and alternative medicine is rapidly increasing in developed countries and in many parts of the world, while uses of traditional medicine remain widespread in developing countries. In Malaysia, safety information with regards to herbs is very limited because there is no universal regulatory system that ensures the safety of phytopharmaceuticals or herbal products (Mohammed, 2006). Most people believe that herbal medicines have no side effects or any potential risks due to their natural origins and are often considered as food supplements, not drugs. This study focused on the herbal plant of *Morinda citrifolia* (locally known as 'mengkudu') which has extensively been used in many countries for its medicinal properties. A number of *in vitro* and *in vivo* studies demonstrate a range of potentially beneficial effects, such as antioxidant and immunomodulatory properties (Olivier & Matthias, 2007). Meanwhile, the increased use of this plant has resulted in concerns over both the efficacy and safety of the product.

TABLE 3
The means organ relative weight of the treatment groups in the male and female rats (mean ± S.E.M)

Parameters	Treatment group					
	Control		Low dose		High dose	
	Male	Female	Male	Female	Male	Female
Body weight	490.4 ± 37.4	265.1 ± 12.1	454.6 ± 14.7	219.1 ± 25.2	477.9 ± 28.6	248.7 ± 6.5
Liver	2.43 ± 0.07	2.75 ± 0.08	2.57 ± 0.08	2.48 ± 0.28	2.48 ± 0.06	2.77 ± 0.10
Kidney	0.56 ± 0.01	0.61 ± 0.02	0.60 ± 0.01	0.54 ± 0.06	0.56 ± 0.02	0.61 ± 0.02
Lungs	0.41 ± 0.03	0.53 ± 0.01	0.38 ± 0.02	0.47 ± 0.05	0.39 ± 0.02	0.57 ± 0.03
Spleen	0.15 ± 0.01	0.18^{a} ± 0.01	0.15 ± 0.01	0.14^{b} ± 0.02	0.15 ± 0.01	0.19^{a} ± 0.01
Heart	0.26 ± 0.01	0.31 ± 0.01	0.26 ± 0.01	0.32 ± 0.03	0.27 ± 0.01	0.32 ± 0.01
Testis	0.58 ± 0.05	n.a	0.53 ± 0.04	n.a	0.61 ± 0.06	n.a

^{a,b}: Means with different superscript/s within the same row differ significantly ($p< 0.05$)

The present study was conducted to evaluate the safety use of *Morinda citrifolia* that was incorporated daily in the diet of male and female Sprague-Dawley rats. As indicated earlier, no deaths and clinical signs of toxicity were observed throughout the experimental period. The consumption of *Morinda citrifolia* was tolerated well and did not produce any general organ or systemic toxicity when fed to the male and female rats at the dose levels of 2000 and 5000 mg/kg/day. One of the indicators for the health status of the experimental animals is an increment in the body weight (Heywood, 1983). In this study, all the rats of both sexes in the treatment and control groups were increased in body weight as they were in the growing stage. At the initial stage of the study, the body weights of the male rats in the low dose group slightly decreased, which could be explained by the attempt of the rats in this group to adjust with the new diet. The decrease in the body weight of the female rats at the end of the experimental period in both the treatment groups as compared to the control could not be determined since the rats were physically healthy and did not show any signs of toxicity. However, the recorded body weights were acceptable for the female rats of this strain at this age. In fact, there were no adverse haematologic effects related to the treatment doses. The cause for the lower WBC in the females of low dose group could not be ascertained since the value was within the normal range of rats of this particular strain and age. In general, clinically low WBC could probably be due to chronic infection, i.e. either bacterial or viral infections. In this study, significantly decreased WBC count was contributed by the decrease in lymphocytes ($2.47 \times 10^3/\mu l$) [data not shown], however these were still within the normal range ($1.64 – 19.5 \times 10^3/\mu l$) of normal healthy rats. Lymphocytes are a type of white blood cell that is responsible for protecting the body against bacterial and viral infections. One of the most common causes of clinically low WBC is an underlying viral infection which can cause a temporary drop in lymphocytes as more

of them are drawn away to fight the infection (David, 2000). Based on the observation made throughout the experimental period, all the rats were clinically healthy and did not show any signs of infection. No treatment-related changes were found in the serum biochemistry of the male and female rats in all the groups. Biochemical measurements, indicative of liver injury such as ALT, AST, ALP, GGT, and total protein, revealed no treatment-related effects. The periportal area of the liver is the first area of the hepatic lobule to be exposed to a toxin being delivered *via* the blood (Huxtable, 1988) and there were no treatment-related changes of the liver enzymes in the male and female rats. The cause for the lower TP in the males of all groups could be explained by the physiological fact since the values were within the normal ranges (60.0–67.0 G/L) for healthy male SD rats. The parameters indicative of kidney functions, such as urea and creatinine (Moshi *et al*., 2001) also showed no treatment-related effects. Organ relative weight measurement is another important guide to assess general toxicity. In particular, changes in the organ weight are indicators of toxicity since these will be affected by the suppression of the body weight (Heywood, 1983). Although the weight of female spleen in the low dose group was significantly lower, the magnitude of the difference is rather small and comparable to the weight of the male spleen in the control and treatment groups, and thus, this cannot be considered clinically relevant. Based on the literature review of the phytochemical content of *Morinda citrifolia*, the histopathological examination was only done on the liver and kidney since these are the two most important organs for detoxification process in the body. The histopathological examination was conducted in all the animals in the control and high dose groups. In the rats that received high doses of *Morinda citrifolia*, no microscopic lesions attributable to the treatment were observed. More importantly, the no treatment-related changes observed in any of the dose groups for the histological examinations demonstrated the absence of toxicity to the liver and kidney.

CONCLUSION

In this study, *Morinda citrifolia* did not show any toxicity even when it was fed at a high dose of 5000 mg/kg body weight. The minor effects observed in both the males and females of the low dose group did not appear to be of toxicological significance. In conclusion, if *Morinda citrifolia* is consumed at the rate of 5000 mg/kg body weight/day, there is likely no chance of developing toxicity, as proven in this study. Therefore, the NOAEL for *Morinda citrifolia* was determined to be greater than 5000 mg/kg body weight per day.

ACKNOWLEDGEMENT

This study was supported by the Intensification of Research Priority Areas (IRPA), Grant No. 01-03-03-0193-EA 001, from the Ministry of Science, Technology and Innovation of Malaysia.

REFERENCES

Chan-Blanco, Y., Fabrice, V., Ana, M.P., Max, R., Jean-Marc, B., & Pierre, B. (2006). The noni fruit (*Morinda citrifolia* L.): A review of agricultural research, nutritional and therapeutic properties. *Journal of Food Composition and Analysis*, *19*, 645-654.

David, M.M. (2000). Hematology of the rat (*Rattus Norvegicus*). In B.E. Feldman, J.G. Zinkl & N.C. Jain (Eds.), *Schalm's veterinary hematology* (5th ed.). (pp. 1210-1218). Baltimore, Maryland: Lippincott Williams & Wilkins.

European Food Safety Authority. (2006). Opinion on a request from the Commission related to the safety of *noni* juice (juice of the fruit of Morinda citrifolia). *European Food Safety Authority Journal*, 1–12.

Heywood, R. (1983). Long term toxicity. In M. Balls, R.J. Riddel & A.N. Worden (Eds.), *Animals and alternatives in toxicity testing* (pp. 79-89). London: Academic Press.

Huxtable, C.R.R. (1988). The liver and exocrine pancreas. In W.F. Robinson & C.R.R. Huxtable (Eds.), *Clinicopathologic principles for*

veterinary medicine (pp. 194-215). Cambridge: Cambridge University Press.

Millonig, G., Staldmann, S., & Vogel, W. (2005). Herbal hepatotoxicity: Acute hepatitis caused by a Noni preparation (*Morinda citrifolia*). *European Journal of Gastroenterology and Hepatology*, *17*, 445-447.

Mohammed, M.A.M. (2006). Effect of *Morinda citrifolia* (linn.) n phase i and ii drug metabolism and its molecular mechanism elucidation in rat liver. Master of Science Thesis, Universiti Sains Malaysia. Malaysia.

Moshi, M.J., Lutale, J.J.K., Rimoy, G.H., Abbas, Z.G., Josiah, R.M., & Andrew, B.M. (2001). The effect of Phyllanthus amarus aqueous extract on blood glucose in non-insulin dependent diabetic patients. *Phytotherapy Research*, *15*, 577-80.

Nelson, S.C. (2001). Noni cultivation in Hawaii. *Fruit and Nuts*, *4*, 1-4.

OECD Guideline 408. (1998). Repeated Dose 90-Day Oral Toxicity Study in Rodents. *OECD Guidelines for Testing of Chemicals*. Retrieved August 20, 2010 from http://www.oecd.org.

Olivier, P., & Matthias, H. (2007). Morinda citrifolia (Noni) fruit – phytochemistry, pharmacology and safety. *Planta Medica*, *73*(3), 191-199.

Ross, I.A. (2001). *Medical plants of the world. Chemical constituents, traditional and modern medical uses*. New Jersey: Humana Press.

Stadlbauer, V., Fickert, P., Lackner, C., Shmerlaib, J., Krisper, P., Trauner, M., & Stauber, R.E. (2005). Hepatotoxicity of NONI juice: Report of two cases. *World Journal of Gastroenterology*, *11*, 4758-4760.

Wang, M.Y., West, B., Jensen, C.J., Nowicki, D., Su, C., Palu, A.K., & Anderson, G. (2002). *Morinda Citrifolia* (Noni): A literature review and recent advance in Noni Research. *Acta Pharmacologica Sinica*, *23*, 1127-1141.

West, B.J., Jensen, C.J., & Westendorf, J. (2006). *Noni* juice is not hepatotoxic. *World Journal of Gastroenterology*, *12*(22), 3616-3619.

Yüce, B., Gülberg, V., Diebold, J., & Gerbes, A.L. (2006). Hepatitis induced by noni juice from Morinda citrifolia: A rare cause of hepatotoxicity or the tip of the iceberg. *Digestion*, *73*, 167-170.