Acute Oral Toxicity Effects of *Momordica Charantia* in Sprague Dawley Rats

R. Nurul Husna, A. Noriham, H. Nooraain, A. H. Azizah, and O. Farah Amna

***Abstract*—*Momordica charantia* is commonly known as bitter gourd, balsam pear or karela is a multi-purpose herb. It is cultivated from different parts of the world and is usually used in traditional medicine. This study was conducted to investigate the acute oral toxicity effects of *Momordica charantia* in Sprague Dawley rats based on OECD Guidelines 423. The extract was administered orally at two different doses of 300 mg/kg and 2000 mg/kg of body weight. The toxicity signs were recorded within the first 24 hours after forced feeding. Both of the treated groups showed dizziness and depression during the first 30 minutes. However, no significant difference of feeding patterns which included water, food intake and body weight gain were observed. Haematological evaluations did not show significant differences in white blood cells count (WBC), mean corpuscular volume (MCV) and mean corpuscular haemoglobin concentration (MCHC) levels. However, red blood cells count (RBC) and packed cell volume (PCV) percentage was significantly lower in rats that received 2000 mg/kg than those of the other two groups. Meanwhile, haemoglobin (Hb) count and the relative liver weight of rats received 2000 mg/kg body weight of extract decreased significantly ($p<0.05$) as compared with the control group. Thus, this study is expected to be beneficial for clinical and traditional applications for safe consumption and to utilize *Momordica charantia* as a remedy at a recommended dosage.**

***Index Terms*—*Momordica charantia*, toxicity evaluation, feeding patterns, haematological parameters.**

I. Introduction

Momordica charantia or bitter melon, grows in the tropical area is popularly consumed as vegetables and has high medicinal values [1], [2]. It is one of the most promising alternative medicines used as anti-HIV, anti-ulcer, anti-inflammatory, antileukemic, anti-microbial, anti-diabetic, and anti-tumor [3]-[5]. Herbal drugs may attract people to consume it due to their effectiveness, relatively low cost and have potential in therapeutic applications without concerning about the toxicity effects it might cause. Investigation on the toxicity profile of *M. charantia* in any applications is very important to ensure the safety of the public upon consuming this plant. Therefore, this study was designed to evaluate the acute oral toxicity effects of ethanolic extract of *Momordica charantia*.

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R. Nurul Husna, A. Noriham, O. Farah Amna, and H. Nooraain are with the Universiti Teknologi MARA (UiTM) 40450 Shah Alam, Selangor, Malaysia (e-mail: husnarosli88@gmail.com, noriham985@salam.uitm.edu.my, nooraain@salam.uitm.edu.my, farahamna88@gmail.com).

A. H. Azizah is with Department at Agro-Biotechnology Institute (ABI), on leave from Universiti Putra Malaysia (UPM) (e-mail: azizahhamid@mosti.gov.my).

II. Methodology

A. Preparation of Samples

Momordica charantia was purchased from wet market in Section 6, Shah Alam, Malaysia. It was washed, cored and sliced thinly. It was then blended using warring blender together with liquid nitrogen to form powder, followed by freeze drying process. The dried sample was collected 5 to 6 days later, weighed and soaked in 80% of ethanol for 3 days. Pure sample was collected by separating the sample and ethanol via vacuum rotary evaporator. The pure sample were freeze dried again and stored in -20 ℃ prior to use.

B. Single-Dose Oral Toxicity Study (14-Days)

The acute oral toxicity study was conducted according to the procedure as described [6].

C. Animal and Feeding Condition

Healthy and non-pregnant adult female Sprague Dawley rats purchased from Chenur Supplier Sdn. Bhd. Kajang, Malaysia were used in this study. The age ranged between 8 to 12 weeks and body weight was between 180-220 grams. The animals were acclimatised for 5 days at standard laboratory conditions: temperature, 22 ℃ ± 3 ℃, relative humidity, 30% ≤ 70% and lighting, 12-h light and 12-h dark. The animals were provided with standard rodent pellets and *ad libitum* supply of water.

D. Experimental Design

A total of 18 female rats (6 rats/group), were randomly selected and marked for individual identification. The test groups included a control group (0.9% saline) and two other treatment groups with dosages at 300 mg/kg and 2000 mg/kg body weight of extract, respectively. The animals were observed and monitored daily for mortality, behaviour and appearance with priority given to the first 4 hours after administration of the extract. Food consumption and water intake were measured daily. However weight gains of the rats were taken weekly.

E. Haematology

On the 14th day of the study, the animals were anesthetized with diethyl ether. The blood was drawn through cardiac puncture and collected into Ethylenediaminetetraacetic acid (EDTA) anticoagulant tubes. The blood were analyzed for several parameters which included red blood cells (RBC) count, white blood cells (WBC) counts and haemoglobin (Hb) content using standard

laboratory methods as described by [7] and packed cell volume (PCV) content as described by [8].

III. Results

No death was observed during the experimental investigation. All of the control and treated rats survived until the end of the treatment period. However, the animals administered with 300 mg/kg and 2000 mg/kg dosage of extracts all had demonstrated symptoms of toxicity which were depression and dizziness for the first 30 minutes after feeding. As the level of dosage increased in the treated groups, there was no significant decreased in trend at $p<0.05$ for body weight gained as compared to control group. Daily food and water intake revealed that there were no significant different between control and treated groups as shown in Table I.

On day 14 prior to anesthetized, the final body weight of individual rats was measured and the blood was collected through cardiac puncture. Table II presented the haematological values which showed no significant differences at $p<0.05$ between control and treated groups for white blood cells (WBC) count mean corpuscular volume (MCV) and mean corpuscular haemoglobin concentration (MCHC). However, there was a dose-related decrease ($p<0.05$) for each red blood cells (RBC) counts, haemoglobin (Hb) and packed cell volume (PCV) contents in the treated groups as compared with the control group. Significant reductions of the above mentioned parameters were recorded for rats treated with 2000 mg/kg of extract.

The target organs collected were measured individually and the relative organ weights were recorded. The results shown in TABLE 3 highlighted insignificant differences of the relative organ weights ($p<0.05$) between control and treated groups except for the relative weight of the liver. A significantly lower liver weight of 2.90 g was recorded among rats treated with 2000 mg/kg body weight of extract as compared to control, 3.52 g and rats that were treated with 300 mg/kg extract, 3.19 g respectively

IV. Discussion

The results obtained from the acute toxicity study showed that the ethanolic extract of *M. charantia* revealed to be safe at 2000 mg/kg of body weight and below. The lethal dose (LD_{50}) can be categorized under class 5 based on OECD Guideline 423. Reference [9] reported that according to the toxicity rating by FAO/WHO Expert Committee on Food Additives [10], if there is no death occurred at 2 g/kg of body weight, and then it is suffice to assume that the substance is non-toxic. In this context, the ethanolic extract of *M. charantia* is considered safe to be consumed at 2000 mg/kg and below for any applications. The slight decrease in body weight of the three groups was likely due to an overnight fasting period prior to blood sampling and may be stress [11] caused by the forced feeding procedure. The correlation decreased in red blood cells (RBC) count, haemoglobin (Hb) and packed cell volume (PCV) counts showed an indication of changes in the rate of RBCs production. From this result, there is a possibility that the extract may have less potential to stimulate erythropoietin released in the kidney [12]. The role of white blood cells is for defense and also a key to diagnose cancer and autoimmune disease [13]. The results of the white blood cells (WBC) counts for control and treated groups were within the reference range which is 1.13-7.49x103/mm3, based on the clinical laboratory parameters as reported by [12]. However, the value was lower in the highest dosage of ethanolic extract of *M. charantia*. In this context, this plant has a potential in pharmaceutical value as it promotes to improve the immune system.

Liver is the main organ in the living systems that functions for detoxification where it makes harmful and not very soluble compound to less harmful and more soluble compounds [13]. Reduction in body and internal organ weights after exposure to the substance are reported to be considered as sensitive indices of toxicity[3], [9], [14], [15]. Hence, the ethanolic extract of *M. charantia* revealed to be slightly toxic as the highest dosage showed several symptoms of toxicity as well as reduction in the weight of the main organ which is the liver. This indicates the presence of toxic constituents in the *M. charantia* extract.

TABLE I: Ffeeding Pattern of Rats Administered with M. Charantia for 14-Days of Observation

Feeding patterns (Mean ± SEM)	Unit	Dose groups, mg/kg		
		Control	300	2000
Water intake	ml/day	27.91 ± 1.46[a]	28.24 ± 1.68[a]	28.20 ± 1.57[a]
Food intake	g/day	16.77 ± 1.03[a]	17.68 ± 0.36[a]	15.63 ± 0.47[a]
Body weight gain	g/week	7.58 ± 1.93[a]	7.08 ± 1.21[a]	6.75 ± 2.30[a]

Mean ± SEM, (n=6)
Parameters on each row with different suffixes are significantly different at $P<0.05$

TABLE II: Haematological Values of Rats Administered with Ethanolic Extraction of M. Charantia for 14-Days

Evaluated parameters (Mean ± SEM)	Unit	Dose groups, mg/kg		
		Control	300	2000
Red blood cells (RBC)	10^6/ mm^3	7.43 ± 0.29[a]	7.14 ± 0.63[a]	5.28 ± 0.47[b]
White blood cells (WBC)	10^3/ mm^3	4.25 ± 1.03[a]	5.12 ± 1.11[a]	3.03 ± 0.39[a]
Haemoglobin (Hb)	g/dL	15.95 ± 0.35[a]	14.85 ± 0.43[ab]	14.30 ± 0.55[b]
Packed cell volume (PCV)	%	55.93 ± 2.46[a]	55.66 ± 2.76[a]	46.46 ± 2.00[b]
Mean corpuscular volume (MCV)	μm^3	76.28 ± 6.00[a]	81.16 ± 8.54[a]	90.78 ± 7.10[a]
Mean corpuscular haemoglobin concentration (MCHC)	%	28.92 ± 1.83[a]	26.92 ± 1.15[a]	30.88 ± 1.02[a]

Mean ± SEM, (n=6)
Parameters on each row with different suffixes are significantly different at $P<0.05$

V. Conclusion

In conclusion, the LD_{50} of the ethanolic extract of *Momordica charantia* is considered safe to be consumed below 2000 mg/kg. However, the study indicates that the highest dosage could provoke the toxic effects to the blood, tissue and vital organ especially liver. Thus, the findings from this study aid in providing more information on the safety level of recommended dosage of ethanolic extract of *Momordica charantia* for further applications or commercialisation.

TABLE III: Relative Organ Weights of Rats in Acute Treatment with Ethanolic Extraction of *M. Charantia*

Organ weights (Mean ± SEM)	Unit	Dose groups, mg/kg		
		Control	300	2000
Heart	g	0.35 ± 0.01[a]	0.35 ± 0.01[a]	0.37 ± 0.02[a]
Liver	g	3.52 ± 0.12[a]	3.19 ± 0.24[ab]	2.90 ± 0.01[b]
Lung	g	0.79 ± 0.09[a]	0.71 ± 0.05[a]	0.83 ± 0.17[a]
Kidney	g	0.75 ± 0.03[a]	0.72 ± 0.04[a]	0.69 ± 0.03[a]
Ovary	g	0.07 ± 0.00[a]	0.07 ± 0.00[a]	0.06 ± 0.00[a]

Mean ± SEM, (n=6)
Parameters on each row with different suffixes are significantly different at $P<0.05$

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R. Nurul Husna was born in Perlis, Malaysia on November 23, 1988. She was graduated from Kedah Matriculation College, Malaysia in Science Biology from 2007-2008 and hold a Bachelor (Hons) of Food Science and Technology from Universiti Teknologi MARA (UiTM), Malaysia from 2008-2011. Currently, she is furthering her study as postgraduate student in Master in Science by research major in food *in vivo* toxicology study from the same university. Hired as a substitute teacher for primary and secondary school for English and Science subjects for 2 years, she had experienced and developed positive relationship with students, parents and school committees. She is now working as research assistant in the same university specialized in plant *in vivo* toxicology study.