

#### **Journal of Medicinal Plants**



Journal homepage: www.jmp.ir

#### **Research Article**

# Protective effect of *Citrullus colocynthis* (L.) Schard. fruit extract on high glucose-induced neurotoxicity in PC-12 cells

Hasan Fallah Huseini<sup>1</sup>, Sina Andalib<sup>2</sup>, Eghbal Jasemi<sup>1</sup>, Farahnaz Khalighi-Sigaroodi<sup>1</sup>, Saeideh Momtaz<sup>1</sup>, Rasoul Mohammadi Savadroodbari<sup>1</sup>, Hadi Salehirad<sup>3</sup>, Mojtaba Ziaee<sup>4,\*</sup>

- <sup>1</sup> Medicinal Plant Research Center, Institute of Medicinal Plants, ACECR, Karaj, Iran
- <sup>2</sup> Zanjan Applied Pharmacology Research Center, Zanjan University of Medical Sciences, Zanjan, Iran
- <sup>3</sup> Faculty of Pharmacy, Tehran University of Medical Sciences, Tehran, Iran
- <sup>4</sup> Medicinal Plants Research Center, Maragheh University of Medical Sciences, Maragheh, Iran

#### ARTICLE INFO

# Keywords: Hyperglycemia C. colocynthis PC-12 cells MTT assay Fractionation Neurotoxicity

#### **ABSTRACT**

Background: Diabetic neuropathy is a consequence of chronic hyperglycemia that leads to neural damage over time. The fruits of Citrullus colocynthis (L.) Schard. (C. colocynthis) have long been used in Iranian traditional medicine for treatment of diabetes. **Objective**: In this study, we investigated the protective effects of *C. colocynthis* against high glucose-induced neurotoxicity in PC-12 cells as a suitable in vitro model for neuronal functions. Methods: The seedless dry fruit powder was extracted with methanol and then dried by rotary evapoartion. Later the obtain extract was fractionated as hexane, chloroform, ethyl acetate, and n-butanol fractions and aqueous residue. HPLC method was used for qualitative analysis of colocynthin in C. colocynthis pulp. The PC-12 cell viability of total extract and fractions of C. colocynthis were evaluated by means of dose and time in high glucose medium in PC-12 cells as a suitable culture model for studying neuronal functions through MTT assay. Results: The PC-12 cell viability significantly decreased in wells containing high glucose, compared with normal glucose treated cells. C. colocynthis extract treatment significantly enhanced the cells viability under toxic high glucose condition in a dose and time depending manner. Methanol extract of C. colocynthis exhibited a protective effect against high glucoseinduced cytotoxicity in PC-12 cells. Conclusion: C. colocynthis has neuroprotective properties against high glucose condition in vitro.

#### 1. Introduction

The main characteristic of diabetes mellitus is increase in blood sugar level due to insufficiency in insulin secretion by pancreas beta-cells or presence of insulin resistance at the cellular level [1]. Chronic hyperglycemia can cause damage to almost all the body nerve called neuropathy, affecting the motor, sensory or autonomic

Abbreviations: MTT, 3-(4,5-Dimethylthiazol-2-Yl)-2,5-Diphenyltetrazolium Bromide; HPLC, High performance liquid chromatography; EDTA, Ethylenediamine tetraacetic acid

doi: 10.52547/jmp.20.80.60

Received 16 May 2021; Received in revised form 28 November 2021; Accepted 29 December 2021

© 2020. Open access. This article is distributed under the terms of the Creative Commons Attribution-NonCommercial 4.0 International License (<a href="https://creativecommons.org/licenses/by-nc/4.0/">https://creativecommons.org/licenses/by-nc/4.0/</a>)

<sup>\*</sup>Corresponding author: ziaee.m@mrgums.ac.ir

nerves. This condition results in undesired and destructive impacts on the digestive system, urinary tract, sexual function, blood vessels, heart, and eyes [2]. It was well established that in hyperglycemia, overproduction of free radicals leads to metabolic dysfunction which allows reactive oxygen species to attack and damage proteins, lipids, and nucleic acids and eventually cause cellular and tissue damage [3]. There is evidence that increased oxygen free radicals due hyperglycemia, is associated with development of apoptosis in nerve cells and consequently neuropathy [3, 4]. Given that, antioxidant therapy may be a proper rational to improve neural protection, particularly in diabetic subjects [5]. Up to date, many studies confirmed the significance of herbal remedies with antioxidant properties in prevention or control of diabetes [6, 7].

C. colocynthis (L.) Schard. (Cucurbitaceae), also known as bitter apple, is a medicinal plant traditionally used for diabetes treatment in Iran [8]. Experimental studies have reported its anti-diabetic and antioxidant properties [9 - 11]. The anti-diabetic and antioxidant effects of C. colocynthis were also observed in clinical trials [12, 13]. In order to provide evidence on mechanism of action of C. colocynthis in diabetic condition in neuronal cells, the protective effect of the methanolic extract and fractions of the fruits of C. colocynthis was investigated in high glucose treated PC-12 cells.

#### 2. Materials and Methods

#### 2.1. Extraction, fractionation and isolation

C. colocynthis fruits were purchased from the local market and authenticated by an expert botanist. A voucher specimen was deposited (No. PMP-3601) in the herbarium of the Faculty of Pharmacy, Tehran University of Medical Sciences, Tehran, Iran. The fruits were washed

using deionized water and dried in the shade at room temperature. The seeds were removed manually from the dried fruit pulp. The dried fruit pulp was grounded and passed through the No. 4 mesh. The plant was then weighed (450 g) and extracted with 2500 ml methanol in percolator for 24 hours. The total methanol extract was dried by rotary evaporator at 50 °C. A portion of 20 g of dried crude extract was dissolve into distilled water and then subjected to a separator funnel. Then, it was fractionated by different solvents with different polarity including hexane, chloroform, ethyl acetate, and *n*-butanol. All fractions were evaporated to dryness at 50 °C using a rotary evaporator [14].

#### 2.2. HPLC analysis of the C. colocynthis pulp

HPLC method was used for qualitative analysis of colocynthin in *C. colocynthis* pulp. For this purpose, powdered *C. colocynthis* pulp (100 mg) was grinded with electronic grinder. 2 ml of methanol was added and shacked slightly by vortex for 30 seconds and placed in the sonicator for 10 min. The solid material was separated by centrifugation in 6000 rpm for 10 min. A determined volume (150 μL) of clear solution was diluted with 850 μl of Millipore water, passed through 0.45 μm PTFE filter and analyzed by HPLC [14].

### 2.3. Assessment the effect of high glucose on PC-12 cell viability MTT assay

Cell culture: The PC-12 cells were obtained from the Pasteur Institute of Iran (Tehran, Iran). DMEM (Dulbecco's Modified Eagle's medium) and FBS (fetal bovine serum) were purchased from Biosera (UK). Pen-strep and trypsin- EDTA were purchased from Gibco (UK). MTT (3-[4, 5-dimethylthiazol-2-yl] 2, 5- diphenyl tetrazolium bromide) was purchased from sigma (Germany). Cells were maintained at 37 °C in a 90 % humid

atmosphere containing 5 %  $CO_2$ . Cells were grown in Dulbecco's modified Eagle's medium (DMEM) with 5 % (v/v) fetal bovine serum (heat-inactivated), 100 units/ml penicillin, and 100  $\mu$ g/ml streptomycin. The cells were subcultured twice a week by gentle scraping.

#### 2.4. MTT cell viability assay

The cell viability was determined using a modified 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium (MTT) assay previously described. Cells were incubated with 5 mg/ml MTT in RPMI, at 37 °C under 5 % CO<sub>2</sub> for 3 h. The blue formazan reduction product, produced by the action of succinate dehydrogenase in cells, was dissolved in dimethylsulfoxide (DMSO), and the optical density was read at 570 nm by an ELISA microplate reader (BioTek, USA) [15]. The concentration required for 50 % inhibition of cell viability (IC<sub>50</sub>) were determined by a nonlinear regression analysis and expressed in mean ± standard error of mean (SEM).

2.5. Effect of high glucose on PC-12 cell viability MTT assay

PC-12 cells seeded in appropriate condition (as mentioned) and the cells were exposed to 13.5 and 27 mM glucose for 24, 48 and 72 h and the MTT cell viability assay was performed accordingly. Since the optimal glucose concentration for PC-12 cell cultures is 4.5 mg/L, we simulated *in vitro* hyperglycemia by increasing the medium glucose level up to 13.5 and 27 mg/ml (three and six fold of the optimal glucose concentration) to investigate the influence of glucose on neuronal cell death [16].

#### 2.6. Total extract treatments

PC-12 cells were plated at the density of 10<sup>3</sup> per well in a 96 micro plate well. The wells were divided into 9 groups (Table 1). Based on results obtained from the previous section, we found that both the concentrations of glucose either 13.5 or 27 mg/ml result in a similar toxicity in PC-12 cells, therefore the concentration of 13.5 mg/ml was selected for this assay.

Table 1. The effective concentration of total extract against cytotoxicity of glucose

Groups	Sample name	Total extract (µg/ml)	Glucose (mg/ml)
1	A0	100	13.5
2	A1	25	13.5
3	A2	2.5	13.5
4	A3	0.25	13.5
5	A4	0.025	13.5
6	G1	0	13.5
7	G2	0	4.5
8	C	0	0

2.6. Assessment of the effect of C. colocynthis total extract and fractions on PC-12 high glucose-induced cell toxicity

At first, we culture cells in normal medium. Following 70 % confluency, were switched from the standard culture (normal glucose DMEM) to the high glucose DMEM overnight (13.5 mg/ml). Based on our pilot study, we found that both the

concentrations of glucose either 13.5 or 27 mg/ml result in a similar toxicity in PC-12 cells, therefore the concentration of 13.5 mg/ml was selected for this assay. The PC-12 cells were treated with different concentrations of the aqueous, methanol, hexane, chloroform and ethyl acetate fractions ranging from 0 to 250  $\mu$ g/ml and the cell viability was investigated after 24, 48 and

72 h. So, we could find the best concentration (IC<sub>50</sub>) of every fractions which show higher protective effect against high glucose.

#### 3. Results

#### 3.1. Extraction, fractionation and isolation

The yield of total methanol extract of the plant was 11.47 %. The yields of the fractions in 20 g of dry methanol extract were presented in Table 2.

#### 3.2. HPLC analysis of the C. colocynthis pulp

The HPLC chromatogram confirmed the presence of the colocynthin peak (RT = 13.277

min) comparison with the study by Shekarchi et al (Fig. 1) [14].

## 3.3. Effect of high glucose on PC-12 cell viability MTT assay

Co-culture of PC-12 cells and 13.5 and 27 mM glucose for 24, 48 and 72 h exhibited toxicity within the cells, reaching a maximal effect after 72 h. Furthermore, we found that concentration of 13.5 and 27 mM show same cytotoxicity and therefore for following experiment we used 13.5 mM glucose for hyperglycemia condition (Fig. 2).

Table 2. The yields of methanol extract and fractions of C. colocynthis

	Methanol	Hexane	Chloroform	Ethyl acetate	Butanol	Aqueous
	Extract	Fraction	Fraction	Fraction	Fraction	Residue
Yield (%)	11.47	1.5	37	3	20.5	38

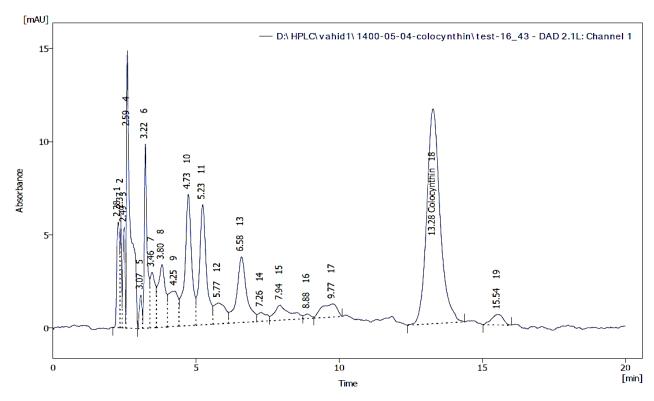


Fig. 1. HPLC Chromatogram of fruit pulp extract of C. colocynthis

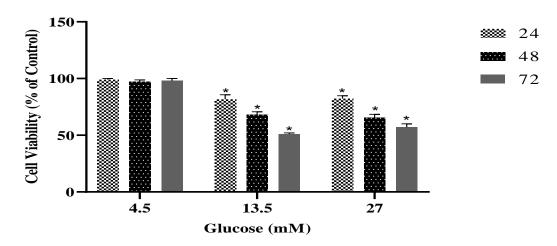
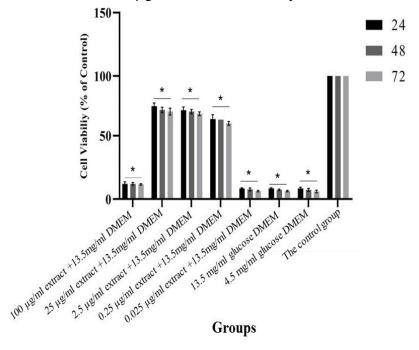


Fig. 2. Effects of glucose concentration and culture time on PC-12 cell viability. Data are presented as mean  $\pm$  SEM (n = 4). The difference between the control group and the treatment group with different concentrations of glucose after 24, 48, and 72 h. significant level: \* P < 0.001.

3.4. Effect of C. colocynthis total extract on glucose-induced cell toxicity

Co-cultivation of G2: 13.5 mg/ml glucose and PC-12 cells led to a significant cytotoxicity. Instead, co-administration of glucose and *C. colocynthis* at concentrations of 2.5 µg/ml,

0.25  $\mu$ g/ml and 0.025  $\mu$ g/ml significantly maintained the PC-12 cell viability and exhibited a positive neuroprotective effect against glucose-induced cell toxicity. However, *C. colocynthis* at concentrations of 100  $\mu$ g/ml was not effective and the cell viability reduced below 10 % (Fig. 3).



**Fig. 3.** Protective effect of total extract against glucose in PC-12 cells after at 24, 48, and 72 h time intervals. Cell viability was measured by MTT assay. Results are reported as the mean S.E.M (n = 4). \* P < 0.001 compared to controls.

3.5. The effect of C. colocynthis fractions on glucose-induced cell toxicity

PC-12 cells were treated with different concentrations of aqueous, methanol, hexane, chloroform and ethyl acetate fractions ranging from 0 to 250  $\mu$ g/ml for 24, 48 and 72 h. Therefore, the most effective concentration of each fraction with the lowest toxicity towards PC-12 cells was selected to be used in further study against high glucose treatment (Table 3).

To elucidate the protective actions of *C. colocynthis* fractions *in vitro*, PC-12 cell viability was assessed under hyperglycemic conditions (13.5 mg/ml glucose). The protective effect of each fraction against cytotoxicity of glucose has shown in Fig. 4. The ethyl acetate and butanol fractions of *C. colocynthis* exhibited the best protective effect against glucose-induced cell toxicity as compared with that of hexane, chloroform and aqueous treated cells.

Table 3. The most effective (lowest cytotoxicity) concentration (μg/ml) of each fraction against PC-12 cells

	Aqueous	Hexane	Chloroform	Ethyl acetate	Butanol
Concentration	125.0	250.0	62.50	125.0	62.50
$(\mu g/ml)$	123.0	250.0	02.30	123.0	02.30

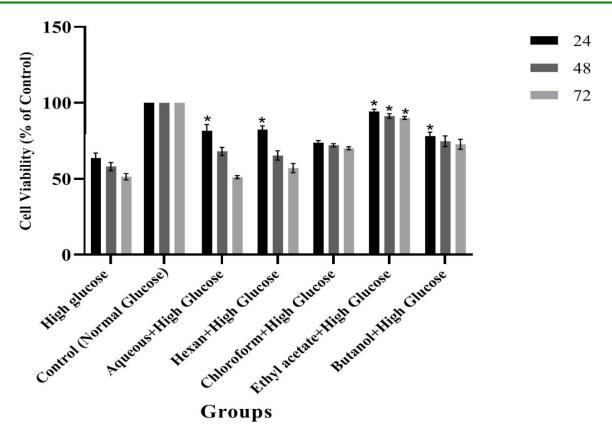


Fig. 4. The protective effect of different *C. colocynthis* fractions on PC-12 cells cultured under hyperglycemic condition. Data are presented as mean  $\pm$  SEM (n = 4). Significant level: \* P < 0.001

#### 4. Discussion

In current study we have examined the protective effect of C. colocynthis against hyperglycemic condition in PC-12 cells by MTT cell viability assay. Aside from hypoglycemic effect of this plant, the study intended to determine whether C. colocynthis has a direct protective effect on nerve cells. Considering our results, the methanolic extract of C. colocynthis at concentrations of 2.5 µg/ml, 0.25 µg/ml, and 0.025 µg/ml significantly protected PC-12 cells against toxic effects of high glucose concentration. Treatment with butanol fraction of this plant at 62.5 µg/ml also significantly reduced the glucose-induced cell toxicity in PC-12 cells.

Mechanism of this protective effect of *C. colocynthis* against high glucose condition is not clearly understood yet. In previous studies on the experimental model of diabetes and clinical trials in type 2 diabetic patients, we have shown that C. colocynthis has antioxidant properties in addition to its hypoglycemic function [8, 11-12].

In this connection the protective effects of *C. colocynthis* on liver, kidneys, and pancreas tissue in STZ-induced diabetic rat reported previously [17].

Nonetheless, it is known that during high glucose treatment production of ROS, one of the major determinant of cell death, lead to apoptosis of PC-12 cells [18]. In addition it is known that in diabetes there are significant functional and metabolic disorders, as a result of hyperglycemia and oxidative stress, which leads to the intensification of violations of the structure of cell membranes [18]. It has been reported that *C. colocynthis* pulp extract possess antioxidant effects in alloxan-induced diabetic rats [19].

#### References

**1.** Fauci AS. Harrison's principles of internal medicine. McGraw-Hill Education; 2015.

#### 5. Conclusion

In the present study, we observed the effect of C. colocynthis in protecting PC-12 cells against toxic effects of high glucose concentrations. Although we could not find the protective mechanisms of C. colocynthis in the PC-12 cell line, there is no doubt that chronic hyperglycemia plays an important role in the development and diabetic exacerbation of neuropathy producing ROS and oxidative stress as an important mediator in the apoptotic pathway. However the protective effects of *C. colocynthis* in the PC-12 cell line may justify its usefulness in the treatment of diabetes and some of its complications if more comprehensive studies confirm it.

#### **Author contributions**

M.Z. and S.A. designed the study and analyzed the results. E.J. and R.M performed the material preparation and data collection. S.M supervised the laboratory work. F. K.S. prepared extracts and performed HPLC. H.F and M.Z. drafted manuscript. All of the authors have read the final manuscript and approved the submission.

#### **Conflict of interest**

The authors declare that there is no conflict of interest.

#### Acknowledgement

This study was financially supported by Medicinal Plants Research Center, Institute of Medicinal Plants, ACECR, Karaj, Iran.

**2.** Russell JW and Zilliox LA. Diabetic neuropathies. *Continuum* (Minneap Minn). 2014;

- 20(5): 1226. doi: 10.1212/01.CON. 0000455884. 29545.d2.
- **3.** Newsholme P, Cruzat VF, Keane KN, Carlessi R and de Bittencourt Jr PIH. Molecular mechanisms of ROS production and oxidative stress in diabetes. *Biochemical J.* 2016; 473(24): 4527-4550.
- **4.** Asmat U, Abad K and Ismail K. Diabetes mellitus and oxidative stress—A concise review. *Saudi Pharmaceutical J.* 2016; 24(5): 547-553.
- **5.** Maritim A, Sanders A and Watkins Iii J. Diabetes, oxidative stress, and antioxidants: a review. *Journal of Biochemical and Molecular Toxicol*. 2003; 17(1): 24-38.
- **6.** Choudhury H, Pandey M, Hua CK, Mun CS, Jing JK, Kong L and Kesharwani P. An update on natural compounds in the remedy of diabetes mellitus: A systematic review. *J. Tradit. Complement. Med.* 2018; 8(3), 361-376. doi: 10.1016/j.jtcme.2017.08.012
- 7. Fallah Huseini H, Abdolghaffari AH, Ahwazi M, Jasemi E, Yaghoobi M and Ziaee M. Topical application of Teucrium polium can improve wound healing in diabetic rats. *Int. J. Low Extrem. Wounds* 2020; 19(2): 132-138.
- **8.** A Z. *Medicinal Plants*. Vol. 5. Tehran, Iran: Tehran University press; 1996.
- **9.** Fallah Huseini H, Kianbakht S, Mousavi R and Aman Zadeh N. Study on Effects of Processing with Vinegar and Saline on Toxicity and Anti-diabetic Property of *Citrullus colocynthis* (L.) Schrad. Fruit Extract in Rats. *Journal of Medicinal Plants* 2011; 4(40): 119-123.
- **10.** Ostovar M, Akbari A, Anbardar MH, Iraji A, Salmanpour M, Ghoran SH, Heydari M and Shams M. Effects of *Citrullus colocynthis* L. in a rat model of diabetic neuropathy. *J. Integrative Medicine* 2020; 18(1): 59-67.
- **11.** Sebbagh N, Cruciani-Guglielmacci C, Ouali F, Berthault M-F, Rouch C, Sari DC and Magnan

- C. Comparative effects of *Citrullus colocynthis*, sunflower and olive oil-enriched diet in streptozotocin-induced diabetes in rats. *Diabetes & Metabolism* 2009; 35(3): 178-184.
- **12.** Fallah Huseini H, Zaree A, Heshmat R, Larijani B, Fakhrzadeh H, Rezaii Sharifabadi R, Naderi G, Zaringhalam J and Shikh Samani A. The effect of *Citrullus colocynthis* (L.) Schrad. fruit on oxidative stress parameters in type II diabetic patients. *J. Med. Plants* 2006; 1(17): 55-60.
- **13.** Yaghoobi M, Miri-Moghaddam E, Navidian A, Nikbakht R, Mehrafarin A and Fallah Huseini H. Safety and Efficacy of Processed *Citrullus colocynthis* L. Fruit in Treatment of Hyperlipidemic Type II Diabetic Patients: A Randomized, Placebo-controlled Clinical Trial. *J. Med. Plants* 2014; 13(52): 81-88.
- **14.** Widyawati PS, Budianta TDW, Kusuma FA and Wijaya EL. Difference of solvent polarity to phytochemical content and antioxidant activity of *Pluchea indicia* less leaves extracts. *International Journal of Pharmacognosy and Phytochemical Res.* 2014; 6(4): 850-855.
- **15.** Kumar P, Nagarajan A and Uchil PD. Analysis of cell viability by the MTT assay. *Cold Spring Harbor Protocols* 2018; 2018(6): pdb. prot095505.
- **16.** Greene LA and Rein G. Synthesis, storage and release of acetylcholine by a noradrenergic pheochromocytoma cell line. *Nature*. 1977; 268(5618): 349-351.
- **17.** Ebrahimi E, Mohammadzadeh G, Mansouri E and Aberomand M. Effects of hydro-alcoholic leaf extract of *Citrullus colocynthis* on biochemical factors and histopathological changes in streptozotocin-induced diabetic rats. *Jundishapur Journal of Natural Pharmaceutical Products* 2016; 11(3): e33214. doi: 10.17795/jjnpp-33214.

[ DOR: 20.1001.1.2717204.2021.20.80.3.0 ]

- **18.** Shakeel M. Recent advances in understanding the role of oxidative stress in diabetic neuropathy. *Diabetes Metab. Syndr.* 2015; 9(4): 373-378. doi: 10.1016/j.dsx.2014.04.029.
- **19.** Kumar S, Kumar D, Saroha K, Singh N and Vashishta B. Antioxidant and free radical scavenging potential of *Citrullus colocynthis* (L.) Schrad. methanolic fruit extract. *Acta Pharmaceutica*. 2008; 58(2): 215-220.

How to cite this article: Fallah Huseini H, Andalib S, Jasemi E, Khalighi-Sigaroodi F, Momtaz S, Mohammadi Savadroodbari R, Salehirad H, Ziaee M. The effect of *Citrullus colocynthis* (L.) Schard. fruit extract on high glucose-induced neurotoxicity in PC-12 cells. *Journal of Medicinal Plants* 2021; 20(80): 60-68.

doi: 10.52547/jmp.20.80.60



## فصلنامه گیاهان دارویی

Journal homepage: www.jmp.ir



مقاله تحقيقاتي

اثر حفاظتی عصاره میوه هندوانه ابوجهل در مقابل اثرات سمیت عصبی گلوکز در رده سلولهای PC-12 حسن فلاح حسینی اسینا عندلیب اقبال جاسمی فلاح خسینی سیگارودی سعیده ممتاز رسول محمدی هادی صالحی راد معتبی ضیائی شدی ضیائی شدی است الله معتبی ضیائی شده معتبی ضیائی شده معتبی ضیائی شده الله معتبی ضیائی شده معتبی ضیائ

ا مركز تحقیقات گیاهان دارویی، پژوهشكاده گیاهان دارویی جهاد دانشگاهی، كرج، ایران

ٔ مرکز تحقیقات داروشناسی کاربردی، دانشگاه علوم پزشکی زنجان، زنجان، ایران

" دانشکاده داروسازی، دانشگاه علوم پزشکی تهران، تهران، ایران

\* مركز تحقیقات گیاهان دارویی، دانشكاده علوم پزشكی مراغه، مراغه، ایران

#### اطلاعات مقاله جكيد

گلواژگان: افزایش قند خون هندوانه ابوجهل سلولهای PC-12 سنجش MTT فراکسیونه کردن سمیت عصبی

مقدمه: نوروپاتی دیابتی از پیامدهای هیپرگلیسمی مزمن است که با گذشت زمان منجر به آسیب عصبی می شود. میوه هندوانه ابوجهل .Citrullus colocynthis (L.) Schard از دیرباز در طب سنتی ایران برای درمان دیابت استفاده می شده است. هدف: در این مطالعه، ما اثرات محافظتی C. colocynthis از گلوکز می در برابر سمیت عصبی ناشی از گلوکز بالا در سلولهای PC-12 به عنوان یک مدل آزمایشگاهی مناسب برای عملکردهای عصبی مورد بررسی قرار دادیم. روش بررسی: میوه خشک بدون دانه با متانول عصاره گیری و سپس با تقطیر در خلاء خشک شد. سپس عصاره بدست آمده به فراکسیونهای هگزانی، کلروفرهی، اتیل استاتی، بوتانول نرمال و باقیمانده آبی تقسیم شد. از کروماتوگرافی مایع با کارایی بالا برای آنالیز کیفی کولوسینتین موجود در پالپ میوه هندوانه ابوجهل استفاده شد. ماندن سلول 12-PC توسط عصاره تام و فراکسیونهای آن با استفاده از دوز و زمان در محیط قند بالا در سلول های PC-12 به عنوان یک مدل مناسب برای مطالعه عملکردهای عصبی از طریق سنجش MTT مورد بررسی قرار گلوکز به میزان قابل توجهی کاهش یافت. اما درمان با عصاره هندوانه ابوجهل بطور قابل توجهی باعث افزایش ماندگاری سلولها در شرایط سمی بالای گلوکز بسته به دوز و زمان شد. عصاره متانولی هندوانه ابوجهل این اثر محافظتی را در برابر سمیت سلولی ناشی از گلوکز بالا در سلولهای PC-12 بهتر نشان داد. نتیجه گیری: هندوانه ابوجهل دارای خواص محافظتی عصبی در برابر شرایط بالای گلوکز در شرایط آزمایشگاهی میباشد.

doi: 10.52547/jmp.20.80.60

منخففها: MTT، ۳- (۵،۴- دی متیل تیازول-۲- ایل)- ۵،۲- دی فنیل تترازولیوم بروماید؛ HPLC، کروماتوگرافی مایع با کارایی بالا؛ EDTA، اتیلن دی آمین تترا استیک اسید

<sup>\*</sup> نو يسنده مسؤول: ziaee.m@mrgums.ac.ir

تاریخ دریافت: ۲۶ اردیبهشت ۱۴۰۰؛ تاریخ دریافت اصلاحات: ۷ آذر ۱۴۰۰؛ تاریخ پذیرش: ۸ آذر ۱۴۰۰

<sup>© 2020.</sup> Open access. This article is distributed under the terms of the Creative Commons Attribution-NonCommercial 4.0 International License (<a href="https://creativecommons.org/licenses/by-nc/4.0/">https://creativecommons.org/licenses/by-nc/4.0/</a>)