

## Original Research Article

# Efficacy and safety of Tian-teng decoction in treating hypertensive emergency

Pengying Yin<sup>1\*</sup>, Huawei Miao<sup>2</sup>, Tan'e Liu<sup>2</sup>, Fenqiao Chen<sup>2</sup>

<sup>1</sup>Emergency Department, <sup>2</sup>Department of Cardiology, Hebei Provincial Hospital of Traditional Chinese Medicine, Hebei, China

\*For correspondence: **Email:** [lucih351@163.com](mailto:lucih351@163.com)

Sent for review: 10 September 2023

Revised accepted: 27 February 2024

### Abstract

**Purpose:** To investigate the efficacy and safety of the traditional Chinese herbal formula (Tian-Teng Decoction) for the treatment of patients with hypertensive emergency.

**Methods:** 120 patients with hypertensive emergency who were treated in Hebei Provincial Hospital of Traditional Chinese Medicine between July 2021 and December 2022 were equally and randomly divided into study and control groups. Patients in the study group received orally Tian-Teng decoction (300 mL divided into two portions administered morning and evening for 2 weeks), while control group received only conventional treatment (sublingual captopril at 12.5 mg twice daily for 2 weeks). Symptoms improvement, changes in blood pressure, onset time, laboratory indicators, clinical manifestations, and adverse reactions were recorded.

**Results:** The study group exhibited significant decrease in blood pressure 30 min after medication ( $p < 0.05$ ). Systolic and diastolic blood pressures were significantly lower in the study group compared to control group at 1, 2, and 3 h after medication. Nitric oxide (NO) was significantly higher, while angiotensin II (Ang II), insulin-like growth factor-1 (IGF-1), angiotensin-converting enzyme (ACE), traditional Chinese medicine syndrome scores, and the incidence of adverse reactions were significantly lower in study group compared to control group ( $p < 0.05$ ).

**Conclusion:** Tian-Teng Decoction demonstrates good efficacy and safety in the treatment of hypertensive emergency. Future studies that incorporate a larger sample size and prolonged observation period to validate the findings of this study are recommended.

**Keywords:** Tian-Teng Decoction, Hypertensive emergency, Efficacy, Medicine safety

This is an Open Access article that uses a funding model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>) and the Budapest Open Access Initiative (<http://www.budapestopenaccessinitiative.org/read>), which permit unrestricted use, distribution, and reproduction in any medium, provided the original work is properly credited.

Tropical Journal of Pharmaceutical Research is indexed by Science Citation Index (SciSearch), Scopus, Web of Science, Chemical Abstracts, Embase, Index Copernicus, EBSCO, African Index Medicus, JournalSeek, Journal Citation Reports/Science Edition, Directory of Open Access Journals (DOAJ), African Journal Online, Bioline International, Open-J-Gate and Pharmacy Abstracts

## INTRODUCTION

Hypertension, as a prevalent chronic metabolic disorder, has gained worldwide attention in the field of global health. Hallmark is the sustained elevation ( $\geq 140/90$  mmHg) of blood pressure, which leads to severe consequences such as cardiovascular and cerebrovascular diseases.

Hypertensive emergency is an acute complication of hypertension, characterized by a rapid increase in blood pressure over a short period, without an immediate life-threatening risk [1]. While not as immediately hazardous as a hypertensive crisis, hypertensive emergency still necessitates timely treatment and medical management to prevent further complications.

Typically, hypertensive emergency is accompanied by symptoms such as headache, dizziness, nausea, vomiting, blurred vision, and palpitations, and patients may experience discomfort or even anxiety. While these symptoms may not worsen hypertensive crisis, the adverse effects of elevated blood pressure are still much present. Therefore, prompt and effective treatment is often necessary to prevent further deterioration [2]. While Western medicine is one of the primary methods for treating hypertension, it requires patients to take medication over a long period to control blood pressure. During this process, patients need to maintain good compliance to ensure treatment effectiveness. However, prolonged use of Western medicine not only raises the risk of potential side effects but may also affect treatment efficacy to differing degrees.

Traditional Chinese medicine (TCM), an integral part of China's ancient medical heritage, holds a wealth of experience in managing hypertension. Among these, Tian-Teng decoction, a traditional TCM formula with a millennia-long history, has been extensively utilized in regulating hypertension and its emergency. The herbal formula of Tian-Teng decoction contains *Gastrodia elata* 10 g, *Uncaria rhynchophylla* 30 g, Chrysanthemum flower 10 g, Eucommia bark 15 g, Achyranthes root 15 g, White peony root 15 g, Cassia seed 15 g, Kudzu root 15 g, Rehmannia root 10 g, Goji berry 10 g, with modifications as needed. In addition to heat-clearing, detoxification, and liver-calming properties, Tian-Teng decoction is believed to effectively lower blood pressure, alleviate symptoms, and to some extent, improve cardiovascular function.

Despite the extensive application of Tian-Teng decoction, its efficacy and safety in treating hypertensive emergency is yet to be systematically validated through clinical study. Therefore, this study is aimed at investigating the efficacy and safety of Tian-Teng decoction in treating patients with hypertensive emergency. This study hopes to provide more reliable evidence for TCM's treatment of hypertensive emergency, thus contributing to the well-being of patients.

## METHODS

### General information

This study employed a randomized controlled method [3] for observational study, aiming to assess the efficacy and safety of Tian-Teng decoction in treating hypertensive emergency.

Patients with hypertensive emergency who were treated in Hebei Provincial Hospital of Traditional Chinese Medicine between July 2021 and December 2022 and met the inclusion criteria were enrolled as study subjects. After excluding subjects who did not meet the inclusion criteria, a total of 120 patients were enrolled, registered, and randomized into study and control groups. Patients in study group received Tian-Teng decoction, while patients in control group received conventional treatment. This study was approved by the Ethics Committee of Hebei Provincial Hospital of Traditional Chinese Medicine (approval no. 2021-06-013) and conducted in line with the provisions in the Declaration of Helsinki [4]. All patients were informed about the study and voluntarily signed an informed consent form.

### Inclusion criteria

The age range was 20 to 70 years, and both males and females were eligible. Patients who met the relevant diagnostic criteria [5] (blood pressure of 140/90 mmHg or higher or ambulatory blood pressure monitoring (HBPM) daytime average or HBPM average of 135/85 mmHg or higher) for hypertensive emergency were included.

### Exclusion criteria

Patients with severe heart, liver and kidney dysfunction, pregnant and lactating women, and those with allergic tendencies were excluded.

### Treatments

Patients in study group received treatment with Tian-Teng decoction. The herbs were decocted with water to obtain 300 mL of filtrate. The decoction was divided into two portions and administered morning and evening, respectively after meals.

Control group received conventional treatment (sublingual administration of captopril produced by Changzhou Pharmaceutical Co., Ltd., National Medical Products Administration approval no. H32023731) at a dose of 12.5 mg, twice per day for 2 weeks.

### Evaluation of parameters/indices

#### Blood pressure monitoring

Systolic and diastolic blood pressure values of study group were measured using an Omron medical electronic blood pressure monitor 5 mins before treatment, 10 mins, 30 mins, and 60 mins

after treatment. Additionally, diastolic and systolic blood pressure values were recorded 1, 2, and 3 h after medication. This was performed once daily for a total of 2 weeks [6].

**Laboratory indices**

Changes in nitric oxide (NO) [7], angiotensin II (Ang II) [8], insulin-like growth factor-1 (IGF-1) [9], and angiotensin-converting enzyme (ACE) [10] levels, were measured and recorded.

**Traditional Chinese Medicine (TCM) syndrome scores**

Traditional Chinese Medicine (TCM) syndrome scores [11] and the incidence of adverse reactions after 2 weeks were recorded. Syndrome scores were divided into four items; headache, palpitations, sensation of warmth in the chest, and restlessness, according to the Guiding Principles for Clinical Research of New Chinese Medicine [12].

**Adverse reactions**

Adverse reactions such as dizziness, nausea, low blood pressure, and dermatitis were monitored and recorded.

**Data analysis**

GraphPad Prism 8 (GraphPad Software, San Diego, CA, USA) was used for image processing, while Statistical Packages for Social Sciences version 26.0 (SPSS Inc., Chicago, USA) software was used for statistical analysis. Measurement data were presented as mean ± standard deviation (SD), and *t*-test was used to compare statistical differences. Count data were presented as percentages (%), while Chi-square test ( $\chi^2$ ) was used to compare statistical differences. *P* < 0.05 was considered statistically significant.

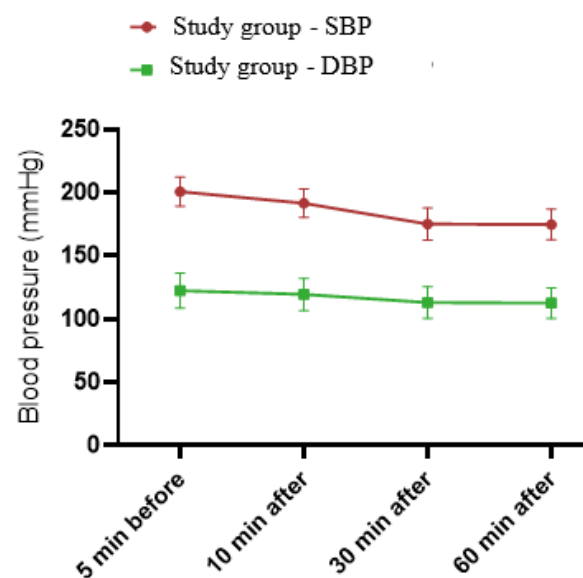
**RESULTS**

**Baseline characteristics**

There was no significant difference in baseline information of subjects in both control and study groups (*p* > 0.05) (Table 1).

**Onset time**

There was a significant reduction in blood pressure in study group 30 mins after medication and remained stable up to 60 mins compared to control group (Figure 1).



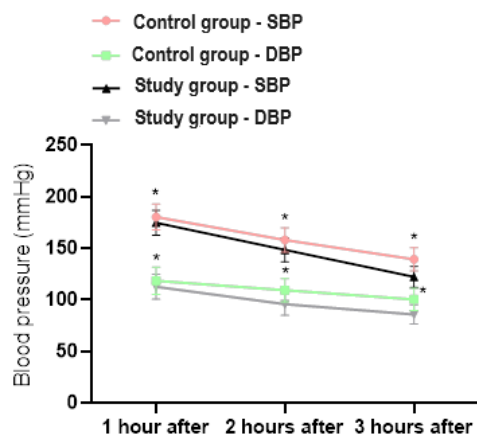
**Figure 1:** Blood pressure reduction in study group after medication

**Blood pressure**

Diastolic and systolic blood pressure in study group at 1, 2, and 3 h after medication were significantly lower compared to control group (*p* < 0.05) (Figure 2).

**Table 1:** Baseline characteristics (mean ± SD) (N = 60 in each group)

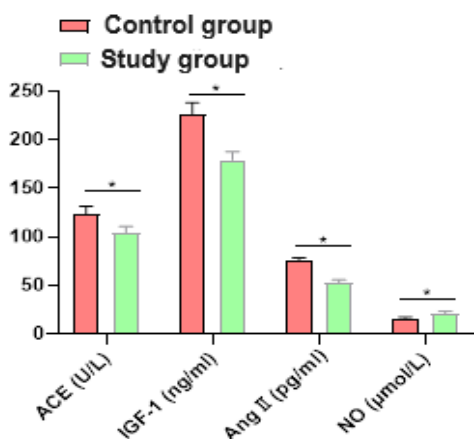
Parameter		Control	Study	T-value	P-value
<b>Gender</b>	Male	35	31	-	-
	Female	25	29	-	-
<b>Age (years)</b>		33-64	30-68	-	-
	Mean	51.44±2.77	51.67±2.52	0.421	0.713
<b>Duration of illness (years)</b>		1-13	1-13	-	-
	Mean	7.22±2.16	7.39±2.71	0.493	0.656
<b>Educational background</b>	High School	16	18	-	-
	Associate Degree	28	27	-	-
	Bachelor Degree	11	13	-	-
	Higher Degrees	5	2	-	-



**Figure 2:** Blood pressure at 1-3 h after medication between the two groups. \* $P < 0.05$  between the two groups

**Laboratory indices**

Levels of Ang II, IGF-1, and ACE in study group after treatment were significantly lower compared to control group, while NO levels were significantly higher compared to control group ( $p < 0.05$ ) (Figure 3).



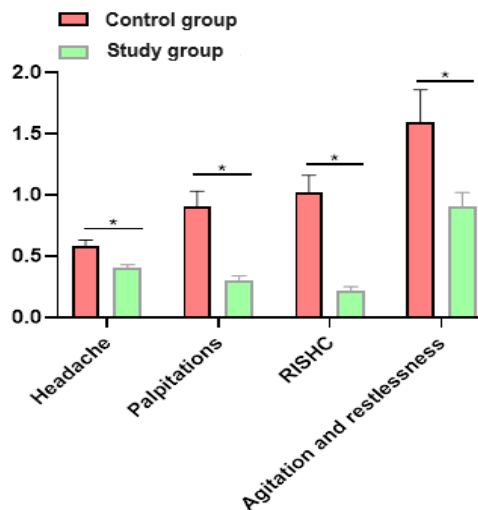
**Figure 3:** Laboratory indices after treatment in both groups. \* $P < 0.05$  between the two groups

**Traditional Chinese medicine syndrome score**

The TCM syndrome scores for patients in the study group after treatment were significantly lower compared to control group ( $p < 0.05$ ; Figure 4).

**Adverse reactions**

Incidence of adverse reactions in study group after treatment (1.67 %) was significantly lower compared to control group (11.67 %,  $p < 0.05$ ), as shown in Table 2.



**Figure 4:** Traditional Chinese Medicine syndrome scores. \* $P < 0.05$  between the two groups. RISHC (Restlessness and irritability with a sensation of heat in the chest)

**Table 2:** Incidence of adverse reactions (N = 60 in both groups) (N, %)

Reactions	Control	Study	$\chi^2$	P-value
Dizziness	3(5%)	1(1.67%)		
Nausea	2(3.33%)	0		
Hypotension	1(1.67%)	0		
Dermatitis	1(1.67%)	0		
Overall incidence	11.67%	1.67%	7.321	0.012

**DISCUSSION**

Hypertensive emergency devoid of immediate threat to life is characterized by a rapid increase in blood pressure within a short period. It is often accompanied by noticeable symptoms such as headaches, dizziness, nausea, vomiting, blurred vision, and palpitations. The underlying causes of hypertensive emergency are multifaceted, including adverse drug reactions, non-compliance with medication, overuse of medication, emotional stress and excessive salt intake [13]. In some cases, emergency may represent an unstable condition of chronic hypertension, requiring prompt intervention to prevent hypertensive crisis. The primary goals in treating hypertensive emergency are rapid blood pressure reduction, symptom relief, and assessing overall condition to determine need for further treatment. While hypertensive emergency typically does not lead to acute danger, untreated cases impact the quality of life, and increase risk of cardiovascular events, which may potentially escalate into a hypertensive crisis. As a result, seeking timely medical attention and adhering to medical advice are crucial for patients experiencing hypertensive emergency [14].

This study extensively investigated the efficacy and safety of Tian-Teng decoction in treating hypertensive emergency. The results demonstrated that significant blood pressure reduction was observed in study group 30 mins after treatment, and remained stable after 60 mins. Moreover, at 1, 2, and 3 h after treatment, patients in study group exhibited more significant blood pressure reduction compared to control group, with improvements in symptoms such as headaches, palpitations, and restlessness. These findings suggest that Tian-Teng rapidly alleviates symptoms of hypertensive emergency within a short time, making it efficacious. It is noteworthy that the onset time for the study group was significantly shorter compared to control group, highlighting a distinct advantage. This may be attributed to the unique components of Tian-Teng, which possess several pharmacological properties such as heat-clearing, detoxification, and liver-qi regulation [15]. These properties may expedite the adjustment of patients' physiological states, leading to rapid symptom improvement. In TCM for hypertension, a commonly utilized method is the principle of modification, which aims to achieve dual objectives of addressing the root causes and alleviating symptoms. Treatment principles emphasize clearing heat, soothing the liver, nourishing the kidneys, and promoting blood circulation, with the ultimate goal of comprehensively regulating the body's balance.

The exquisite combination of herbs in this formula includes principal herbs like *Gastrodia* and *Uncaria*, which have a liver-soothing effect, and minister herbs like *Abolboda* and *Gardenia* that guide the blood downward, enhancing the therapeutic effect. Assistant herbs like *Eucommia*, *White Peony*, *Rehmannia*, and *Loranthus* contribute to nourishing liver and kidney functions [16], while *Night-Blooming Cereus* and *Salvia miltiorrhiza* play roles in promoting blood circulation and resolving stasis. Concurrently, *Angelica sinensis* aids in spleen health and blood regulation. Through the comprehensive application of these herbs, a synergistic effect is achieved, encompassing smoother blood flow, balanced spleen and liver functions, nourished kidneys, and other multifaceted outcomes to fundamentally adjust functional state, promoting blood circulation, balanced endocrine function, and achieve a sustained and comprehensive therapeutic effect on hypertension.

Furthermore, results of this study demonstrated that the post-treatment level of NO (nitric oxide) in study group was higher compared to control group, while levels of angiotensin II (Ang II),

insulin-like growth factor-1 (IGF-1), and angiotensin-converting enzyme (ACE) were lower in study group. Previous study [17] has shown that under the influence of ACE, renin is transformed into Ang II, leading to increased peripheral vascular resistance, contraction of small arterial smooth muscles, and subsequent increase in blood volume. This plays a crucial role in the pathogenesis of hypertension. Moreover, Ang II is a key effector molecule of the renin-angiotensin system, which may lead to myocardial fibrosis and have adverse effects on the heart. Nitric oxide, a substance secreted by vascular endothelial cells, exerts a strong but transient vasodilatory effect and is also an important mediator in cardiac function. However, inadequate vasodilation is also a significant contributing factor to hypertension. Insulin-like growth factor-1 (IGF-1) is a multifunctional cell proliferation regulator that promotes vascular remodeling, accelerates blood pressure elevation, and increases Ang II expression, thereby accelerating pathological changes in blood vessels and myocardium. The imbalance between IGF-1 and NO is closely related to the development of hypertension [18]. The results of this study not only demonstrated the precise effectiveness of Tian-Teng decoction in treating hypertension but also affirmed the role of captopril.

In modern pharmacological studies, it has been found that Tian-Teng decoction dilates coronary arteries, and microvessels and improves prognosis. Simultaneously, it effectively inhibits the occurrence of myocardial fibrosis, thereby reducing the risk of cardiovascular diseases associated with hypertension. Captopril, an angiotensin-converting enzyme inhibitor, effectively inhibits the activity of ACE in systemic circulation, which aids in gradually reducing the production of angiotensin II. This process significantly attenuates the vasoconstrictive effect, leading to a gradual reduction in peripheral resistance. Moreover, captopril also reduces the release of norepinephrine and lowers the activity of the central sympathetic nervous system. These combined effects contribute to effective blood pressure control and better therapeutic outcomes. Sublingual administration allows for rapid absorption of the drug through the sublingual mucosa, leading to a swift onset of therapeutic effects. This approach not only avoids gastrointestinal irritation but is also convenient and easy to implement. Sublingual administration not only saves time compared to intravenous infusion but also mitigates the risks associated with unstable infusion rates [19]. Especially in pre-hospital complex emergencies, this method is particularly

applicable and better meets the demands of emergency treatment. Western medicine treatment often requires patients to take medication for extended periods, relying on patient compliance, while short-term treatment with Tian-Teng decoction may enhance treatment adherence. Patients in study group exhibited good tolerance and safety during treatment with the modified Tian-Teng decoction, without causing significant adverse reactions such as hypotension. This, to some extent, reduces potential risks patients may face during treatment.

### Limitations of the study

The sample size was relatively small, and the observation period was relatively short, which might have affected the results.

### CONCLUSION

Tian-Teng decoction alleviates symptoms of hypertensive emergency by potentially exerting effects such as *clearing heat* and toxins, *tonifying* the liver and subduing *yang* to regulate physiological functions with a lower incidence of adverse effects. Future studies that incorporate a larger sample size and prolonged observation period to establish the findings of this study are recommended.

### DECLARATIONS

#### Acknowledgements

None provided.

#### Funding

None provided.

#### Ethical approval

None provided.

#### Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

#### Conflict of Interest

No conflict of interest associated with this work.

#### Contribution of Authors

The authors declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by them.

### Open Access

This is an Open Access article that uses a funding model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>) and the Budapest Open Access Initiative (<http://www.budapestopenaccessinitiative.org/read>), which permit unrestricted use, distribution, and reproduction in any medium, provided the original work is properly credited.

### REFERENCES

1. Astarita A, Covella M, Vallelonga F, Cesareo M, Totaro S, Ventre L, Aprà F, Veglio F, Milan A. Hypertensive emergencies and urgencies in emergency departments: a systematic review and meta-analysis. *J Hypertens* 2020 38(7): 1203-1210.
2. Rossi GP, Rossitto G, Maifredini C, Barchitta A, Bettella A, Cerruti L, Latella R, Ruzza L, Sabini B, Vigolo S et al. Modern management of hypertensive emergencies. *High Blood Press Cardiovasc Prev* 2022; 29(1): 33-40.
3. Hariton E, Locascio JJ. Randomized controlled trials - the gold standard for effectiveness research: Study design: Randomized controlled trials. *BJOG* 2018 125(13): 1716.
4. World Medical Association. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. *JAMA* 2013; 310(20): 2191-2194.
5. Hypertension in adults: Diagnosis and management. London: National Institute for Health and Care Excellence (NICE); 2023; 21. (NICE Guideline, No. 136.) Available from: <https://www.ncbi.nlm.nih.gov/books/NBK547161/>
6. Rehman S, Hashmi MF, Nelson VL. Blood pressure measurement. Updated 2022 Dec 28. In: StatPearls Internet. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK482189/>
7. Ghasemi A, Zahediasl S, Azizi F. Reference values for serum nitric oxide metabolites in an adult population. *Clin Biochem* 2010; 43(1-2): 89-94.
8. Catt KJ, Cain MD, Zimmet PZ, Cran E. Blood angiotensin II levels of normal and hypertensive subjects. *Br Med J* 1969; 1(5647): 819-821.
9. Chanson P, Arnoux A, Mavromati M, Brailly-Tabard S, Massart C, Young J, Piketty ML, Souberbielle JC. VARIETE Investigators. Reference values for IGF-I serum concentrations: Comparison of six

- immunoassays. *J Clin Endocrinol Metab* 2016; 101(9): 3450-3458.
10. Ghanbari H, Dehghani A, Feizi A, Amirkhani A, Pourazizi M. Serum level of the angiotensin-converting enzyme in patients with idiopathic acute optic neuritis: A case-control study. *Scientifica (Cairo)* 2020; 2020: 4867420.
  11. Huang Z, Miao J, Chen J, Zhong Y, Yang S, Ma Y, Wen C. A traditional Chinese medicine syndrome classification model based on cross-feature generation by convolution neural network: Model development and validation. *JMIR Med Inform* 2022; 10(4): e29290.
  12. Zheng XY. *Guiding Principles for Clinical Research of New Chinese Medicine (Trial)*. China Medical Science and Technology Press, Beijing. 2002.
  13. Brathwaite L, Reif M. Hypertensive emergencies: A review of common presentations and treatment options. *Cardiol Clin* 2019; 37(3): 275-286.
  14. Paini A, Aggiusti C, Bertacchini F, Agabiti Rosei C, Maruelli G, Arnoldi C, Cappellini S, Muiesan ML, Salvetti M. Definitions and epidemiological aspects of hypertensive urgencies and emergencies. *High Blood Press Cardiovasc Prev* 2018; 25(3): 241-244.
  15. Zhang G, Yang G, Deng Y, Zhao X, Yang Y, Rao J, Wang W, Liu X, He J, Lv L. Ameliorative effects of Xue-Fu-Zhu-Yu decoction, Tian-Ma-Gou-Teng-Yin and Wen-Dan decoction on myocardial fibrosis in a hypertensive rat mode. *BMC Complement Altern Med* 2016; 16: 56.
  16. Chen PJ, Sheen LY. *Gastrodiae Rhizoma (tiān má): A review of biological activity and antidepressant mechanisms*. *J Tradit Complement Med* 2011; 1(1): 31-40.
  17. Patel VB, Zhong JC, Grant MB, Oudit GY. Role of the ACE2/angiotensin 1-7 axis of the renin-angiotensin system in heart failure. *Circ Res* 2016; 118(8): 1313-1326.
  18. Muniyappa R, Walsh MF, Rangi JS, Zayas RM, Standley PR, Ram JL, Sowers JR. Insulin-like growth factor 1 increases vascular smooth muscle nitric oxide production. *Life Sci* 1997; 61(9): 925-931.
  19. Hua S. Advances in nanoparticulate drug delivery approaches for sublingual and buccal administration. *Front Pharmacol* 2019; 10: 1328.