Original Article

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Comparative Effect of Cinnamon and Ibuprofen for Treatment of Primary Dysmenorrhea: A Randomized Double-Blind Clinical Trial

Obstetrics and Gynaecology Section

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ABSTRACT

Background and Aims: Primary dysmenorrheal has a negative impact on women's quality of life. The purpose of this study was to compare the effect of Cinnamon and Ibuprofen for treatment of primary dysmenorrheal in a sample of Iranian female college students from Ilam University of Medical Sciences (western Iran).

Materials and Methods: In a randomized, double-blind trial, out of 114, control group received placebo (empty capsules contain starch, TDS, n= 38) a test group received Ibuprofen (capsule containing 400mg Ibuprofen, TDS, n=38), or another test group received Cinnamon (capsule containing 420 mg Cinnamon, TDS, n= 38) in 24 h. To determine severity of pain, we used the VAS scale. Pain intensity and duration of pain were monitored in the group during first 72 h of cycle.

Results: The mean pain severity score and mean duration of pain in Ibuprofen and Cinnamon were less than placebo group respectively ($p< 0.001$). Of 4 hours after the intervention there were no statistically significant differences between the Cinnamon and placebo group ($p> 0.05$). Of eight hours after the intervention, the mean pain severity in the cinnamon group was significantly lower than placebo group ($p< 0.001$). At various time intervals the mean pain severity in the Ibuprofen group were significantly less than Cinnamon and placebo groups ($p< 0.001$).

Conclusion: Cinnamon compared with placebo significantly reduced the severity and duration of pain during menstruation, but this effect was lower compared with Ibuprofen. Cinnamon can be regarded as a safe and effective treatment for primary dysmenorrhea. More researches are recommended to study the efficacy of Cinnamon on reducing menstrual bleeding.

Keywords: Medicinal herbal, Menstruation, Pain

INTRODUCTION

Primary dysmenorrhea is one of the most common gynecologic disorders [1-3]. Prostaglandin production by ovulation is the main cause of primary dysmenorrhea [4-6]. Dysmenorrhoea may affect more than half of menstruating women [7]. Primary dysmenorrhea is defined as a cyclic and painful cramps pelvic occurring just before or during menstruation that derange daily activities [8]. Prevalence in different populations is between 50% and 90% and in Iran between 74% and 86.1% [9,10]. Primary dysmenorrhea is a common cause of absenteeism from work, education or refer to doctor, that these subjects may lead to decreased efficacy of occupational and educational [11]. Although dysmenorrhea is not life threatening, it can have adverse effects on quality of life [12].

In the USA, dysmenorrhea annually economic loss is 600 million work hours and $ 2 billion [13,14]. In an epidemiological study of 664 school students in Egypt, about 75% of the students have dysmenorrhea, rated mild in 55.3%, moderate in 30%, and severe in 14.7% [15]. In a study of women students, 42% of people have a session's absence from teaching or leave of daily activities due to dysmenorrhea. The study suggests that 50% of girls believe that their dysmenorrhea impair daily activities [16]. Several methods such as drugs (including OCP consumption and non-steroidal anti-inflammatory drugs ,{NSAID}), non pharmacological (including exercise, heat therapy, acupuncture and trans-electrical nerve stimulation (TENS), dietary supplements (vitamins E,B ,C and Ca, Mg) and medicinal herbal used in the treatment of primary dysmenorrheal [17-20]. Synthetic drugs, especially in long-term administration are side effects. Nausea, stomach irritation, ulcers, renal papillary necrosis, and decrease renal blood flow are the side effects of prostaglandin synthesis inhibitors [21]. On the other hand, most of the young girls have no intention of using hormones to decrease of pain. Today regarding effects of chemical drugs, the use of medicinal herbal in the treatment of diseases, have drawn the researcher's attention. Medicinal plants play an abundance role in human health care. More than 80% of people in developing countries used the complementary and alternative medications for treatment health conditions [22]. One of these herbal medicine and alternative therapies which recognized for its biological properties is *Cinnamon Zeylancium* that has much application in medicine but has not been sufficiently documented [23]. *Cinnamomum Zeylancium*, from Lauraceae family has been used as a popular spice in food of Asian, South America, and the Caribbean people not only to improve the food and drinks taste but also in traditional and modern medicines [24-32]. Therefore due to the lack of comprehensive studies in this field in Iran, and because of the importance of economic and social aspects of dysmenorrhea and acceptability and availability of traditional medicines, the aim of this study was to compare the effect of Cinnamon and Ibuprofen for treatment of primary dysmenorrheal in a sample of Iranian female college students from Ilam University of Medical Sciences (western Iran). The study hypothesis was: Cinnamon is effective on dysmenorrhea. The effect of Cinnamon on dysmenorrhea different with Ibuprofen.

MATERIALS AND METHODS

This is an experimental study that was performed at the Ilam University of Medical Sciences (western Iran) during the year Dec 2013 to Dec 2014. The statistical population included all the female college students that were living in dormitories. The study was approved by the Institutional Ethics Committee, and informed consent was obtained from all samples (Ethical code / 92/H/184, date: 13/Dec/2012). Also this study was registered at the Iranian Registry of Clinical Trials (IRCT2013122114668N2).

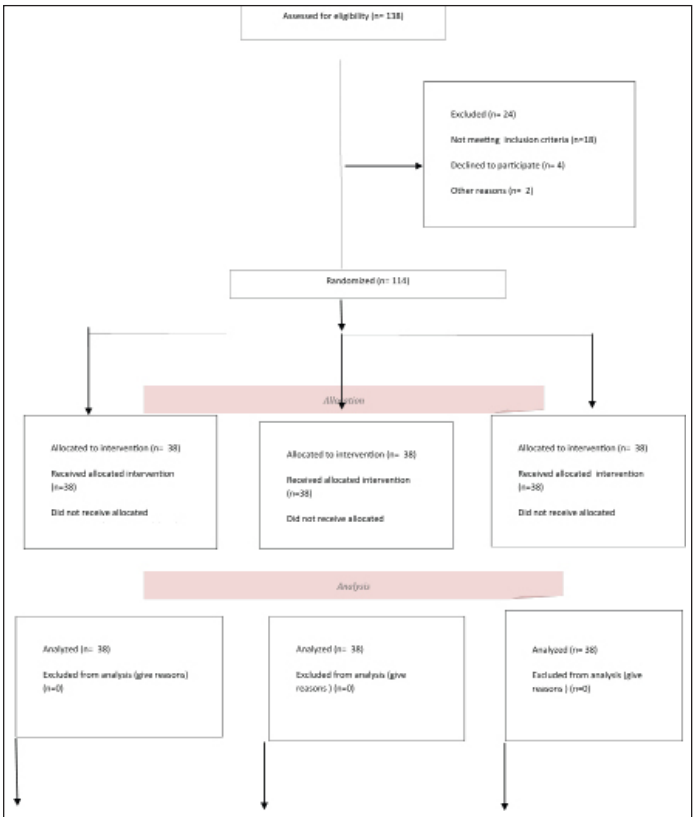
The sample size was calculated using the information obtained from a pilot study with 10 patients and the following formula:

$n= (z_1+z_2)^2(2s^2)/d^2= 38, \quad Z_1 = 1.96, \quad Z_2=0.84, S= 1.67, d = 1.1$

S (An estimate of the standard deviation of VAS in the groups that 1.67 were obtained in a pilot study). d (The minimum of mean difference VAS between groups that show significant. difference and obtained 1.1).

A simple random sampling design was used [Table/Fig-1]. After getting written permission from the school of nursing and midwifery, researcher visited the students of dormitories and objectives of the study were explained to them. Then from interested students that have inclusion criteria using simple random sampling of the number of the students the residence were divided into three groups: placebo, Ibuprofen and cinnamon.

In a randomized, double-blind trial, out of 114, control group received placebo (empty capsules contain starch, TDS, n= 38) a test group received Ibuprofen (capsule containing 400mg Ibuprofen, TDS, n=38), or another test group received Cinnamon (capsule containing 420 mg Cinnamon, TDS, n= 38) in 24 h. Placebo and test drugs was placed in a sealed envelope and then coded the subjects with one the third party was given to subjects. For blind study the order of use and shape of capsules was similar in the three groups. Cinnamon powder was provided from an Iranian company, NAB ROZ (herbal code: 0236110120400479). Then the Cinnamon capsules were prepared based on copulating process [33] in institute of pharmacology in Ilam University of Medical Science.



[Table/Fig-1]: Flow chart

Characteristic	Placebo (n=38)	Ibuprofen (n=38)	Cinnamon (n=38)	p-value
	Mean±SD	Mean±SD	Mean±SD	
Age (year)	1.5± 21.3	1.1±20.8	1.1±20.7	0.135
Age of menarche (year)	0.8±13.4	1.3±13.8	0.8±13.3	0.116
Cycle (day)	1.5±27.8	1.3±27.8	1.5±27.4	0.487
Age of dysmenorrheal (year)	0.9±14.6	1±14.8	0.5±14.3	0.476
Duration of bleeding (day)	1.1±5.8	1±5.9	1.3± 6.3	0.090

[Table/Fig-2]: Characteristics of the participants

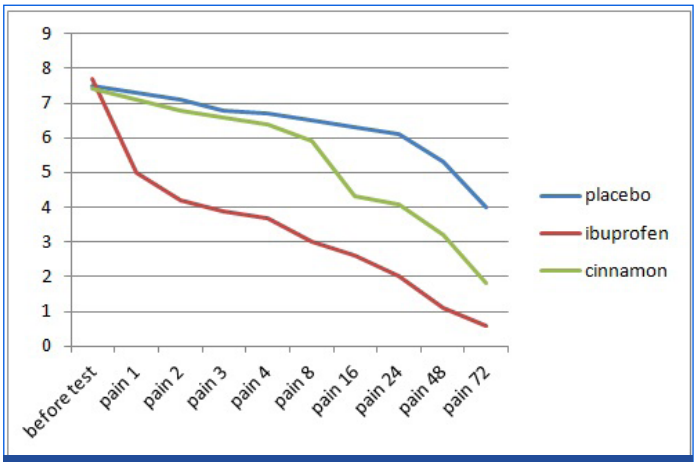
The inclusion criteria included age 18-30, regular menstrual cycles ,moderate primary dysmenorrhea, lack of chronic diseases, not having symptoms such as burning, itching, abnormal vaginal discharge, lack of pelvic inflammatory disease, tumor and fibroma, the lack of recent stressors and BMI [19-26]. The exclusion criteria were the use of OCP contraceptive, medicines or plants allergy and mild dysmenorrhea. We used the Visual Analogue Scale (VAS) to determine severity of pain and Cox Menstrual Scale to determine duration of pain. VAS rating is a standard tool for evaluating of pain severity having ratings from 0 to 10. 0 means no pain and 10 means the maximum pain in this scale. Pain intensity and duration of pain were monitored in the group during first 72 h of cycle. Severity of pain was assessed using VAS before test and after test at different time intervals viz, 1, 2, 3, 4, 8, 16, 24, 48 and 72 h in the groups. Duration of pain was assessed once daily. Collected data were analysed using the statistical software (SPSS, Ver.16). Descriptive statistics, t-test, Man-Whitney and one-way ANOVA test were performed to analyse the results.

RESULTS

Baseline characteristics are shown in [Table/Fig-2]. None of the 114 enrolled female college students was withdrawn for any reason. Samples characteristics were not different among the treatment groups (p> 0.5) [Table/Fig-2].

Characteristic	Placebo (n=38)	Ibuprofen (n=38)	Cinnamon (n=38)	p-value
Pain score by VAS at various intervals (hours)	M±SD	M±SD	M±SD	
Before treatment	1±7.5	0.8±7.7	1±7.4	0.569
1 h after intervention	7.3±0.6	5.0±0.9	7.1±0.7	< 0.001
2 h after intervention	7.1±0.9	4.2±0.5	6.8±0.7	< 0.001
3 h after intervention	6.8±0.7	3.9±0.7	6.6±0.4	< 0.001
4 h after intervention	6.7±0.7	3.7±0.7	6.4±0.6	< 0.001
8 h after intervention	6.5±0.7	3.0±0.2	5.9±0.9	< 0.001
16 h after intervention	6.3±0.4	2.6±0.5	4.3±0.7	< 0.001
24 h after intervention	6.1±0.4	2.0±0.1	4.1±0.5	< 0.001
48 h after intervention	5.3±0.6	1.1±0.3	3.2±0.6	< 0.001
72h after intervention	4.0±0.3	0.6±0.6	1.8±0.4	< 0.001

[Table/Fig-3]: Outcome of severity of pain in groups



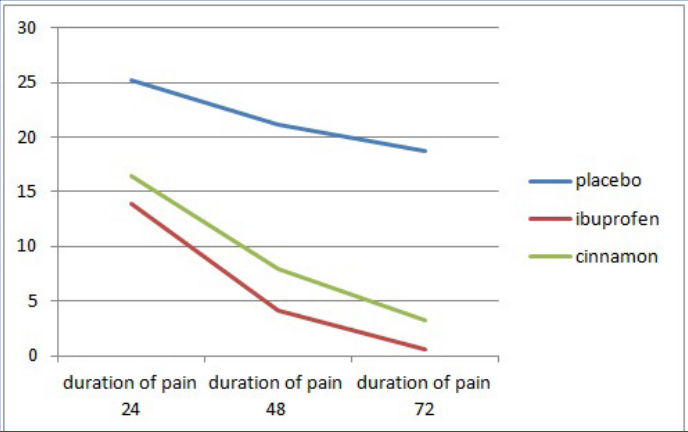
[Table/Fig-4]: Severity of pain in groups

Cinnamon (n=38)	Ibuprofen (n=38)	Placebo (n=38)	Outcome Parameters	p-value
Duration of pain (min)	Mean±SD	Mean±SD	Mean±SD	
Before treatment	2.3±27.2	2.8±27.2	2.3±26.5	0.359
24 h after intervention	16.5±1.6	13.9±1.5	25.2±1.9	< 0.001
48 h after intervention	8.0±0.9	4.2±0.7	21.2±1.5	< 0.001
72h after intervention	3.2±0.4	0.6±0.4	18.7±1.3	< 0.001

[Table/Fig-5]: Outcome of duration of pain

One-way ANOVA test showed that the mean pain severity score in Ibuprofen and Cinnamon were less than placebo group respectively at various time intervals (p< 0.001) [Table/Fig-3,4]. Mean duration of pain in Ibuprofen and Cinnamon were significantly less than placebo group respectively at various time intervals (p< 0.001) [Table/Fig-5,6].

According to LSD and Tukey test to 4 h after the intervention, although the mean pain severity in the cinnamon group was lower than placebo group but there was no statistically significant differences between the two groups (p> 0.05). Of 8 hours after the intervention, the mean pain severity in the cinnamon group was significantly lower than placebo group, (p< 0.001). At various time intervals the mean pain severity in the Ibuprofen group was significantly less than cinnamon and placebo groups (p< 0.001) [Table/Fig-7].



[Table/Fig-6]: Duration of pain in group

Outcome parameters	Between group		p-value	
			LSD	Tukey
1 h after intervention	Placebo	Ibuprofen	< 0.001	< 0.001
		cinnamon	0.382	0.655
2 h after intervention	Placebo	Ibuprofen	< 0.001	< 0.001
		cinnamon	0.101	0.228
3 h after intervention	Placebo	Ibuprofen	< 0.001	< 0.001
		cinnamon	0.131	0.285
4 h after intervention	Placebo	Ibuprofen	< 0.001	< 0.001
		cinnamon	0.061	0.145
8 h after intervention	Placebo	Ibuprofen	< 0.001	< 0.001
		cinnamon	< 0.001	0.001
16 h after intervention	Placebo	Ibuprofen	< 0.001	< 0.001
		cinnamon	< 0.001	< 0.001
24 h after intervention	Placebo	Ibuprofen	< 0.001	< 0.001
		cinnamon	< 0.001	< 0.001
48 h after intervention	Placebo	Ibuprofen	< 0.001	< 0.001
		cinnamon	< 0.001	< 0.001
72 h after intervention	Placebo	Ibuprofen	< 0.001	< 0.001
		cinnamon	< 0.001	< 0.001

[Table/Fig-7]: Outcome of severity of pain between groups

DISCUSSION

Primary dysmenorrhea has a negative impact on women's quality of life. Our results suggest that both Cinnamon and Ibuprofen reduce pain but the effect of Cinnamon was lower than Ibuprofen. In this study we found that Cinnamon of 8h after intervention, significantly decreased severity of pain, although of 4h after intervention there was no significant differences. Therefore Cinnamon is improving the severity of primary dysmenorrhea. This finding is consistent with previous study of the effect of herbal medicines such as *Cumin* [34], *Thymus Vulgaris, Achillea Millefolium* [35] *Fennel* [36,37] *Matricaria Recutita* [38] *Rosa Damascena* Extract [39] and *Zingiber Officinale* [40] in the treatment of dysmenorrhea.

Primary dysmenorrhea is caused by an increase in the synthesis and release of prostaglandins, particularly PGF2 from the uterine endometrium during the menstrual period. This prostaglandin in turn causes contraction of smooth muscles in many adjacent tissues. Uterine smooth muscle contractions cause colicky pains, spasmodic and labor-like pains in the lower abdomen and lower back pain that is characteristic of the dysmenorrhea. Also, prostaglandin secretion causes smooth muscle contraction of gastric-Intestinal tract, that can lead to nausea, vomiting and diarrhea [7,41-43]. Herbal medicines by reducing the level of prostaglandins, nitric oxide modulation, increased levels of beta-endorphin, calcium channel blocking, and improve circulation, is effective in the treatment of dysmenorrhea [44,45].

Cinnamon is a commonly used spice and flavoring for thousands of years in the world [46]. Research in vitro and in vivo studies in animals and humans, have shown numerous beneficial effects of *Cinnamon Zeylanicum* on health included diarrhea, as an astringent, antimicrobial, anti-inflammatory, antioxidant, germicide, analgesic, insecticidal antiseptic, antispasmodic, dyspeptic complaints, for chronic bronchitis, treatment of impotence, frigidity, dyspnea, inflammation of the eye, antimicrobial properties, leukorrhea, vaginitis, rheumatism, and neuralgia, as well as wounds and toothaches, cold and flu but have not been sufficiently documented [8,22,47]. Information about the mechanism of action for *Cinnamon Zeylanicum* on primary dysmenorrheal is little [48]. The oil extracted from the branches of the Cinnamon plant has anti-inflammatory activity. Two of the major compounds of essential oil extracted from Cinnamon are Cinnamaldehyde 90% and eugenol is 5-18%. Cinnamaldehyde has been reported to have an antispasmodic effect. Also, eugenol can prevent biosynthesis of prostaglandins and reduce inflammation. The results of the literature did not have any reported significant adverse events and toxic effects when Cinnamon is used in doses of 1-6 g per day [20,22,49]. In this study to reduce the potential of allergy we used a total dose of 2.5 g daily (in three divided doses) that was effective on primary dysmenorrhea and no side effects were found with this dose of Cinnamon. However, toxicology trials [5,22] performed with high doses demonstrated that the oil of this plant caused irritation of the mucous membranes and provoked hematuria.

Anti - inflammatory drugs such as NSAIDs are used for pain relive in dysmenorrhea. These drugs are antagonists to the prostaglandins which are the source of dysmenorrheal pain [5]. This was the first clinical trial on the effects of Cinnamon on primary dysmenorrhea of female college students in Iran, which were the strengths of this study. Some of the factors influencing pain intensity and other symptoms with primary dysmenorrhea such as culture, genetic disparity and nutrition were uncontrollable, which were the weak point of this study.

CONCLUSION

The research results suggest that, Cinnamon as compared significantly reduces the severity and duration of pain during menstruation, but this effect is less compared to that of Ibuprofen. Due to the lack of adverse events in this study, Cinnamon can be used as a safe and non-pharmacological treatment for primary dysmenorrheal pain in young girls. More researches for the efficacy of Cinnamon, with a larger statistical population, are recommended.

REFERENCES

[1] Marzouk TM, El-Nemer AMR, Baraka HN. The Effect of Aromatherapy Abdominal Massage on Alleviating Menstrual Pain in Nursing Students: A Prospective Randomized Cross-Over Study. *Journal of Alternative and Complementary Medicine*. 2013;2013:742421, 1-6.

[2] Raphkin Aj, Howard CN. pelvic pain and Dysmenorrhea. In: Berek and Novak's gynecology: Lippincott Williams & Wilkins; 2007. pp. 506-34.

[3] Ozgoli G, Goli M, Moattar F. Comparison of effects of ginger, mefenamic acid, and ibuprofen on pain in women with primary dysmenorrheal. *Journal of Alternative and Complementary Medicine*. 2009;15(2):129–32.
[4] Decherney AH, Nathan L. Current Obstetrics & Gynecologic Diagnosis & Treatment. 9th ed. *Mc Grow-Hill. New York*. 2003. Pp.342.
[5] Zdanski de Souza A, Costa Mendieta M, Hohenberger G, Melo Silva M, Ceolin T, Heck R. Menstrual cramps: A new therapeutic alternative care through medicinal plants. *Health*. 2013;5(7):1106-09.
[6] Durain D. Primary dysmenorrhea: assessment and management update. Journal of Midwifery and Women's Health. 2004;49(6):520–27.
[7] SMA Zaidi, K Khatoon, KM Aslam. Role of herbal medicine in Ussuruttams (Dysmenorrhoea). *J Acad Indus Res*. 2012;1(3):113.
[8] Unsal A, Ayranci U, Tozun M, Arslan G, Calik E. Prevalence of dysmenorrhea and its effect on quality of life among a group of female university students. *Upsala journal of medical sciences*. 2010;115(2):138-45.
[9] Ziaei S, Zakeri M, Kazemnejad A. A randomised controlled trial of vitamin E in the treatment of primary dysmenorrhoea. *BJOG*. 2005;112(4):466-69.
[10] Drosdzol A, Skrzypulec V. Dysmenorrhea in pediatric and adolescent gynaecology. *Ginekol Pol*. 2008;79(7):499-503.
[11] Edmonds DK, editor. Dewhur's textbook of obstetrics and gynecology for postgraduates. 6th edition. London: *Blackwell Science*, 1999. pp. 414.
[12] French L. Dysmenorrhea. *American family physician*. 2005;71(2):285-91.
[13] Weissman AM, Hartz AJ, Hansen MD, Johnson SR. The natural history of primary dysmenorrhoea: a longitudinal study. *BJOG*. 2004;111(4):345-52.
[14] Slap GB. Menstrual disorders. In adolescence. *Best Practice & Research Clinical Obstetrics & Gynaecology*. 2003;17(1):75-92.
[15] El-Gilany AH, Badawi K, El-Fedawy S. Epidemiology of dysmenorrhoea among adolescent students in Mansoura, Egypt. *Eastern Mediterranean Health Journal*. 2005;11(1-2):155–63.
[16] French L. Dysmenorrhea in adolescents: diagnosis and treatment. *Paediatr Drugs*. 2008;10(1):1-7.
[17] Dawood MY. Primary Dysmenorrhea: advances in pathogenesis and management. *Obestet & Gynecol*. 2006;108(2):428-41.
[18] Bernard ND, Scillia AR. Diet and sex hormone binding globulin for dysmenorrhea and PMS. *Obstet & Gynecol*. 2000;95(2):245-50.
[19] Proctor ML, Smith Co, Fergnhor CM. Trans cutaneous electrical nerve stimulation and acupuncture for primary dysmenorrhea. *Cochrane Databas of Systematic Review*. (1); 2003, CD: 120 -23.
[20] Jaafarpour M, Khani A , Javadifar N, Taghinejad H, Mahmoudi R, Saadipour KH. The Analgesic Effect of Transcutaneous Electrical Nerve Stimulation (TENS) on Caesarean Under Spinal Anaesthesia. *JCDR*. 2008;(3):815-19.
[21] Ryan KJ, Berkowitz RS, Barbieri RL, Dunaif A. Kistner's Gynecology & Women's Health. 17th Edition. *Golban Medical Publication*. 1999. Pp. 62-63.
[22] Medagama AB, Bandara R. The use of Complementary and Alternative Medicines (CAMs) in the treatment of diabetes mellitus: is continued use safe and effective? *Medagama and Bandara Nutrition Journal*. 2014;13(102):1-9.
[23] Oliveira J de A, Da Silva ICG, Trindade LA, Lima EO, Carlo HL, Cavalcanti AL, et al. Safety and Tolerability of Essential Oil from Cinnamomum zeylanicum Blume Leaves with Action on Oral Candidosis and Its Effect on the Physical Properties of the Acrylic Resin. *Evidence-Based Complementary and Alternative Medicine*. 2014;325670:10.
[24] Badalzadeh R, Shaghagh M, Mohammadi M, Dehghan G, Mohammadi Z. The Effect of Cinnamon Extract and Long-Term Aerobic Training on Heart Function, Biochemical Alterations and Lipid Profile Following Exhaustive Exercise in Male Rats. *Adv Pharm Bull*. 2014;4(Suppl 2):515-20.
[25] Chen L, Yang Y, Yuan P, Yang Y, Chen K, Jia Q, et al. Immunosuppressive Effects of A-Type Procyanidin Oligomers from Cinnamomum tamala. *Evidence-Based Complementary and Alternative Medicine*. 2014;365258:9.
[26] Wani KD, Kadu BS, Mansara P, Gupta P, Deore AV, Chikate RC, et al. Synthesis, Characterization and In Vitro Study of Biocompatible Cinnamaldehyde Functionalized Magnetite Nanoparticles (CPGF Nps) For Hyperthermia and Drug Delivery Applications in Breast Cancer. *PLOS ONE*. 2014; 9(9):e107315,1-13.
[27] Wickenberg J, Lindstedt S, Nilsson J , Hlebowicz J. Cassia cinnamon does not change the insulin sensitivity or the liver enzymes in subjects with impaired glucose tolerance. *Nutrition Journal*. 2014;13:96.
[28] Vakili AR, Khorrami B, Danesh Mesgaran M, Parand E. The effect of thyme and cinnamon essential oil on performance rumen fermentation and blood metabolites in Holstein calves consuming high concentrate diet. *Asian Australas J Anim Sci*. 2013;26(7):935-45.
[29] Piovezan M, Uchida NS, Da Silva AF, Grespan R, Santos PR, Silva EL, et al. Effect of cinnamon essential oil and cinnamaldehyde on Salmonella Saintpaul biofilm on a stainless steel surface. *J Gen Appl Microbiol*. 2014;60:119-21.
[30] Rao PV, Gan SH. Cinnamon: A Multifaceted Medicinal Plant. *Evidence-Based Complementary and Alternative Medicine*. 2014; 642942:12.
[31] Vangalapati M, Sree Satya N, Surya Prakash D, Avanigadda S. A review on pharmacological activities and clinical effects of cinnamon species. *Research Journal of Pharmaceutical, Biological and Chemical Sciences*. 2012;3(1):653–63.
[32] Jakhetia V, Patel R, Khatri P. Cinnamon: a pharmacological review. *Journal of Advanced Scientific Research*. 2010;1(2):19–12.
[33] Remington. The Science and Practice of Pharmacy. Edited by Allen, Loyd V., Jr. 22nd edition.
[34] Hejazi SH, Amin GH, Mahmoudi M, Movaghar M. Comparison of herbal and chemical drugs on Primary Dysmenorrhea. *Journal of Nursing and Midwifery School of Shaheed Beheshti University of Medical Sciences*. 2002;12(42):23-27.
[35] Doubova SV, Morales HR, Hernández SF, del Carmen Martínez-García M, de Cossío Ortiz MG, Soto, et al. Effect of a Psidii guajavae folium extract in the treatment of primary dysmenorrhea: a randomized clinical trial. *Journal of Ethnopharmacology*. 2007;21:305-10.
[36] Khorshidi N. Clinical of essential fennel on primary dysmenorrhea. *Iranian Journal of Pharmaceutical*. 2003;2:89–93.
[37] Namavar Jahromi B, Tartifizadeh A, Khabnadideh S. Comparison of fennel and mefenamic acid for treatment of primary dysmenorrheal. *Int J Gynecol Obstet*. 2003;80(2):153–57.
[38] Astin JA. Why patients use alternative medicine: results of a national study. *Journal of American Medical Association*. 1998;279:1548-53.
[39] Bani S, Hasanpour S , Mousavi Z , Mostafa Garehbaghi P, Gojazadeh M. The Effect of Rosa Damascena Extract on Primary Dysmenorrhea: A Double-blind Cross-over Clinical Trial. *Iran Red Cres Med J*. 2014;16(1):e14643.
[40] Kotani N. Analgesic effect of a herbal medicine for treatment of primary dysmenorrhea. *Am J Chinese Med*. 1997;25(2):205–12.
[41] Lee L, Chen P, Lee K, Kaur J. Menstruation among adolescent girls in Malaysia: a cross-sectional school survey. *Singapore medical journal*. 2006;47(10):869-74.
[42] Dawood MY, Khan-Dawood FS. Clinical efficacy and differential inhibition of menstrual fluid prostaglandin F 2α in a randomized, double-blind, crossover treatment with placebo, acetaminophen, and ibuprofen in primary dysmenorrhea. *American journal of obstetrics and gynecology*. 2007;196(1):35,1-5.
[43] Harel Z. Dysmenorrhea in adolescents and young adults: etiology and management. *Journal of Pediatric and Adolescent Gynecology*. 2006;19(6):363–71.
[44] Jia W, Wang X, Xu D, Zhao A, Zhang Y. Common traditional Chinese medicinal herbs for dysmenorrhea. *Phytotherapy Research*. 2006;20(10):819-24.
[45] Sangal A. Role of cinnamon as beneficial antidiabetic food adjunct: a review. *Advances* in *Applied Science Research*. 2011;2(4):440-50.
[46] Mondal S, Pahan K. Cinnamon Ameliorates Experimental Allergic Encephalomyelitis in Mice via Regulatory T Cells: Implications for Multiple Sclerosis Therapy. *PLOS ONE*. 2015;10(1):e0116566.
[47] Tung YT, Yen PL, Lin CY, Chang ST. Antiinflammatory activities of essential oils and their constituents from different provenances of indigenous cinnamon (Cinnamomumosmophloeum) leaves. *Pharmaceutical Biology*. 2010;48(10):1130–36.
[48] Camacho S, Michlig S, Senarclens-Bezençon CD, Meylan J, Meystre J, Pezzoli M, et al. Anti-Obesity and Anti-Hyperglycemic Effects of Cinnamaldehyde via altered Ghrelin Secretion and Functional impact on Food Intake and Gastric Emptying. *SCIENTIFIC REPORTS*. 2015;5:7919. DOI: 10.1038/ srep07919, 1-10.
[49] Ranasinghe P, Jayawardana R, Galappaththy P, Constantine GR, de Vas Gunawardana N, Katulanda P. Efficacy and safety of "true" cinnamon (Cinnamomum zeylanicum) as a pharmaceutical agent in diabetes: a systematic review and meta analysis. *Diabetic Medicine*. 2012;29(12):1480–92.

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