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Review Article

The Role of Iranian Medicinal Plants of the Asteraceae Family in Pain Therapy: A Systematic Review

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Abstract

Asteraceae or Compositae is considered as one of the main flowering plants around the world which presently have more than 23,600 accepted species from 1,620 genera and 13 subfamilies. The present study aims to systematically review the role of Iranian medicinal plants of the family Asteraceae in pain therapy. We searched several databases, including Scopus, PubMed, Web of Science, EMBASE, Google Scholar, MagIran, and SID without time limitation for publications related to antinociceptive effects of Iranian medicinal herbs of the Ateraceae family. Studies in any language were entered in the search phase if they had an English abstract. Of the 1080 papers obtained from all of the databases up to 2020, 20 articles were reliable and were scrutinized. The most abundant parts of these plants are aerial parts (17 papers, 85%). Based on the obtained results, the most abundant products were hydroalcohol extract (10 papers, 45.5%) and essential oils (8 papers, 40%) of the medicinal herbs of the Asteraceae family. The most frequently tests used were formalin test (77.3%), followed by writhing test (54.5%) and tail-flick test (36.4%). The findings of the present review demonstrated that the Iranian medicinal herbs of the Asteraceae family are generally used to treat and reduce pain. Although herbs in this family may be considered as alternative agents for pain treatment, further studies are required to clear the accurate anti-nociceptive mechanisms as well as toxicity of these plants in human subjects.

Keywords: Antinociceptive, Herbal medicines, Extract, Essential oil, Iran, Asteraceae family

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Introduction

Pain is widely known as an unpleasant mental and emotional condition that is along with promising or actual tissue damage followed by harmful heat, stretch, electrical flow, necrosis, surgical interventions, trauma, etc. (1, 2). At present, antinociceptives or analgesics are categorized into two major groups: (i) opioid drugs which act through activating opioid receptors; (ii) non-steroidal anti-inflammatory drugs (NSAIDs) which constrain prostaglandin synthesis through the inhibition of the cyclooxygenase enzyme (3-5).

Although these drugs are characterized by high efficacy, there have been some limitations and side effects, including sedation, nausea, vomiting,

respiratory and cardiovascular depression, etc. in recent years (5, 6). Consequently, finding a new agent with considerable efficacy and low toxicity is required; whereas medicinal plants can be important sources (5-8).

In recent centuries, medicinal herbs have been recommended due to having natural effective derivatives for preventing or treating conditions associated with pain (9-12). Asteraceae or Compositae is considered as one of the main flowering plants around the world which presently have more than 23,600 accepted species from 1,620 genera and 13 subfamilies (13). Based on certain reports presented in recent years, a wide range of pharmacological and therapeutic properties such as antioxidant, anti-inflammatory, anticancer, and antimicrobial properties have been attributed to the plants in Asteraceae family (13). Previous studies have demonstrated that the main secondary metabolites produced from plants in the Asteraceae family are flavonoids and terpenoids; whereas these compounds have exhibited various biological activities in modern medicine (14-16). This research aimed to systematically review the role of Iranian medicinal plants of the family Asteraceae in pain therapy.

Methods

Search strategy: To carry out this research, we searched several databases, including Scopus, PubMed, Web of Science, EMBASE, Google Scholar, MagIran, and SID without time limitation for publications worldwide related to antinociceptive effects of all Iranian medicinal herbs in the Asteraceae family in order to identify all relevant published articles. Studies in any language were entered in the search phase if they had an English abstract. The words and terms were used as a syntax with specific tags of each database. The searched words and terms were: “herbal medicine”, “medicinal plants”, “antinociceptive”, “analgesic”, “Asteraceae”, “extract”, “essential oil”, “pain”, and “Iran” (Fig. 1.).

Selection of Studies: Initially, the papers were imported to the EndNote X9 software (Thomson Reuters, New York, NY, USA) and duplicate studies were deleted. Afterwards, three independent authors examined the titles and abstracts of the studies and then the relevant studies were included for further analysis. The same authors carefully read the studies and the eligible studies with adequate inclusion criteria were selected. The corresponding author resolved any disagreement between the authors.

Exclusion Criteria: Exclusion criteria included insufficient information, having only an abstract, failure to match methods with results, and inaccurate interpretation of results.

Data Extraction: Three independent authors extracted the information from the selected articles and, if needed, the differences were resolved by the corresponding author. The extracted data included nanoparticles, type of nanoparticles, in combination or loaded with other drugs, type of study, and important results.

Results and Discussion

Of the 1080 papers obtained from all of the databases up to 2020, 20 articles were reliable and were scrutinized (Table. 1). The most abundant parts of these plants were aerial parts (17 papers, 85%). Based on the obtained results, the most abundant product was hydroalcohol extract (10 papers, 45.5%) and essential oils (8 papers, 40%) of medicinal herbs of the Asteraceae family. The most tests used were formalin test (77.3%), followed by writhing test (54.5%) and tail-flick test (36.4%).

Today, drugs used to relieve pain are divided into two groups: narcotics (such as opioids) and non-narcotics (such as salicylates and corticosteroids). Although they show high efficacy, the use of these drugs is subject to some limitations due to adverse and serious side effects (5-8).

The history of treatment of diseases with medicinal plants dates back to the history of human life on Earth. The tendency of the society to use herbal medicines and treatments as well as natural products in general has been increasing, particularly in recent years (12, 37). Moreover, the most important causes are the proof of the destructive and side effects of chemical drugs on the one hand and the creation of environmental pollution that threatens the planet on the other hand (10-12). Currently, 25% of the drugs in the world pharmaceutical market are of plant origin. At the same time, according to the World Health Organization,

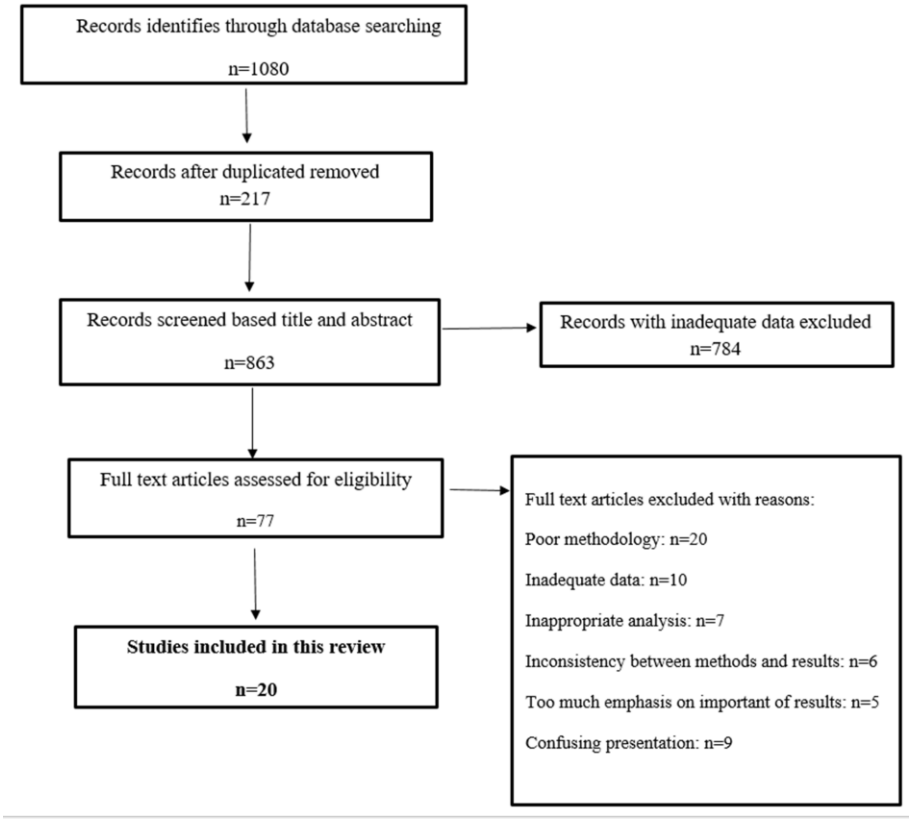

Figure 1. Flowchart for Describing the Study Design Process.

about 80% of the world's population live in developing and poor countries. Due to the high cost of synthetic drugs and their lack of availability and side effects, the main medical needs of these countries are fulfilled from medicinal plants (38, 39).

According to the review reports, Asteraceae as one of the biggest family of herbs demonstrated pharmacological and therapeutic properties such as antioxidant, anti-inflammatory, anticancer, and antimicrobial properties that have been attributed to the plants in the Asteraceae family (13). The results of our review showed that from 1080 papers obtained from all of the databases up to 2020, 20 articles were reliable and were scrutinized. The most abundant parts of these plants are aerial parts (17 papers, 85%). Based on the obtained results, the most abundant product was hydroalcohol extract (10 papers, 45.5%) and essential oils (8 papers, 40%) of medicinal herbs of the Asteraceae family. The most tests used were formalin test (77.3%), followed by writhing test (54.5%) and tail-flick test (36.4%). Previous studies have demonstrated that the main secondary metabolites produced from plants in the Asteraceae family are flavonoids and terpenoids; whereas these compounds showed various biological activities such as analgesic or antinociceptive in pain management (13-15).

Flavonoids are considered as one of the main groups of polyphenolic compounds in vegetables and fruits. In general, flavonoids are divided into three classes of compounds, i.e. (i) flavones (flavone, apigenin, and luteolin), (ii) flavonols (quercetin, kaempferol, myricetin, and fisetin), and (iii) flavanones (flavanone, hesperetin, and naringenin) (40). Flavonoids are abundant in plants of the Asteraceae family that have potent analgesic effects (41). Considering the possible antinociceptive mechanisms of flavonoids, previous studies exhibited that these compounds through crossing brain-blood barrier can control pain via various mechanisms such as affecting gamma-amino butyric acid (GABA) A, opioid, a-adrenergic receptors and inhibiting enzymes related to inflammation in the brain. Furthermore, reviews showed that flavonoids, through inhibiting cyclooxygenase in tissues and

subsequently inhibiting prostaglandins (PG) synthesis are able to control pain (41-43).

Table 1: The Iranian Medicinal Plants of the Asteraceae Family Used for Pain Treatment

Plant	Extraction	The Used Part	Pain Test Type	Outcome	Ref.
Artemisia dracunculus L.	Ethanolic extract	Aerial parts	Formalin, hot-plate, and writhing tests	The ethanolic extract (50 and 100 mg/kg) reduced both phases of pain in the formalin test. The extract (50 and 100 mg/kg) showed antinociceptive activity against acetic acid-induced writhing and hot-plate test.	(17)
Calendula officinalis L.	Hydroethanol extract	Aerial parts	Hot water tail immersion and acetic acid writhing tests	The results of the present study indicated that aqueous extract demonstrated significant differences compared to the control and standard groups in all tests.	(18)
Tanacetum Sonbolii L.	Hydroalcohol extracts	Aerial parts	Formalin tests	At the doses of 150 and 300 mg/kg, significant antinociception in phase 2 was produced. Moreover, at the doses of 600, 900 and 1200 mg/kg antinociceptive effects were induced in phase 1 and phase 2.	(19)
Artemisia dracunculus L.	Essential oil	Aerial parts	Formalin, hot-plate, and writhing tests	At the doses of 100 and 300 mg/kg, reduced the pain response was significantly reduced in the first and second phases of the formalin test, respectively. In the hot-plate test, a significant analgesic activity by increasing latency time was observed. Furthermore, (89, 95, 97 and 97%) the nociception produced by acetic acid was significantly inhibited.	(20)
Artemisia absinthium L.	Hydroalcohol extracts	Aerial parts	Tail flick test	The extract produced antinociceptive effect (at 4 and 6% W/V) concentration in tail flick model.	(21)

Tanacetum Fisherae L.	Essential oil	Aerial parts	Formalin test	The essential oil doses dependently reduced licking and flinching numbers and also pain score in the late (15-35 min) and recovery phases (35-60 min) of formalin test (p0.05) in the early (0-5 min) phase and interphase (5-15 min).	(22)
Achillea millefolium L.	Hydroalcohol extracts	Aerial parts	Formalin test	The extract encapsulated in liposome reduced the nociceptive behavior induced by the use of formalin.	(23
Artemisia absinthium L.	Essential oil	Aerial parts	Acetic acid-induced writhing, formalin and hot plate tests	The essential oil produced significantly decreased the number of writhing in acetic acid-induced writhing model and increased the response latency in hot plate test after 30 min. Moreover, the nociceptive response in the formalin test was significantly suppressed in a dose-dependent manner, while the impact on the late phase was more noticeable.	(24)
Artemisia sieberi L.	Essential oil	Fruits	Formalin test	All doses of A. sieberi fruits essential oil induced antinociceptive activity during the second stage of the formalin test. However, the greatest effect belonged to the dose of 0.8 mg/kg.	(25)
Artemisia aucheri Boiss	Essential oil	Aerial parts	Acetic acid-induced writhing, and hot plate tests	The essential oil remarkably reduced the number of acetic acid-induced writhes in mice in comparison with animals that received vehicle only. Moreover, it showed a central analgesic effect as evidenced by a noticeable increase in reaction time in the hot plate method.	(26)
Gundelia tournefortii L.	Hydroalcohol extracts	Aerial parts	Formalin test	At the doses of 0.3, 0.6, 1.2, and 2.4 g/kg, the pain sensation in the formalin test was reduced ($p < 0.001$ in both phases).	(27)
Inula helenium L.	Hydroalcohol extracts	Aerial parts	Tail-flick, writhing and formalin tests	At the dose of 300 mg/kg, significant antinociceptive effect ($p<0.01$) was	(28)

				observed in writhing (28.21±1.34) and tail-flick (5.11±1.34) tests, in comparison with the control group (41.22±4.12). In the formalin test, pain score was reduced using 100 mg/kg extract from 2.17±0.21 in the control group to 0.53±0.24, in the chronic phase.	
Artemisia persica Boiss	Essential oil	Aerial parts	Formalin and tail immersion tests	At a dose of 50, 75, and 100mg/kg remarkably reduced the duration of paw licking, clopping, and lifting in the first and second phases of formalin test. Furthermore, at the dose of 100mg/kg, the pain response time in the tail immersion test was significantly increased.	(29)
Tanacetum parthenium L.	Hydroalcohol extracts	Aerial parts	Writhing test	At the dose of 40 mg/kg, the pain response was significantly reduced.	(30)
Tanacetum balsamita L.	Essential oil	Aerial parts	Formalin, writhing, and tail-flick tests.	It has been shown that the essential oil at doses of 10-100 mg/ has significant analgesic effects.	(31)
Inula britannica L.	Essential oil	Flower	Acetic acid-induced writhing, tail-flick, formalin tests	At the dose of 100 mg/kg, antinociceptive effects were observed in comparison with the control group.	(32)
Lactuca sativa L.	Methanol/petroleum ether extract	Seed	Tail-flick, formalin tests	The extract demonstrated a time- and dose-dependent antinociceptive activity in the formalin test. However, we did not observe any analgesic effect in tail-flick test up to the highest dose used (6 g/kg).	(33)
Sonchus asper L.	Hydroalcoholic extract	Aerial parts	Writhing, tail-flick, and formalin-, and glutamate-induced paw licking tests.	At the dose of 300 mg/kg, a significant analgesic effects in the tail-flick, writhing and glutamate-induced paw licking tests were observed. Moreover, the dose of 100 mg/kg of significantly reduced the pain scores in the tonic phase of the formalin test.	(34)

Erigeron acer L.	Hydroalcoholic extract	Aerial parts	Writhing, tail-flick and formalin tests	The extract at the dose of 300 mg/kg exhibited a remarkable antinociceptive activity in writhing and tail-flick with P<0.01 and the chronic phase of formalin test (P<0.001).	(35)
Matricaria chamomilla L.	Hydroalcoholic extract	Aerial parts	Formalin and hot plate tests	At the doses of 5-50 g/kg, an analgesic effect on chronic pain induced by the secondary phase of the formalin test was observed.	(36)

Terpenes or isoprenoids are the largest group of phytochemicals which are found in a wide range of plants such as herbs of the Asteraceae family. Reviews reported that terpenoids (sesquiterpenoids, monoterpenoids, diterpenoids, etc.) have numerous biological and pharmacological activities such as anti-inflammatory, anticancer, antioxidant, and antimicrobial activities (45, 46). In the case of the possible analgesic mechanisms of terpenoids, several studies have shown that these compound represent the antinociceptive activities through some pathways, e.g. (i) stopping swelling and bleeding, and reducing pain, (ii) inhibiting PGE2, IL-6 production, COX-2 activity, (iii) blockading Na+ channels, (iv) Inhibiting nerve transmission in cortical nerve cells and dorsal root ganglion cells, (v) and reducing membrane currents by inhibitory effect on Na+ channels currents in dorsal root ganglion neurons (46). These factors demonstrated that analgesic and anti-nociceptive properties of medicinal herbs of the Asteraceae family may be attributed to the presence of these phytochemicals in plants.

Conclusion

The findings of the present review demonstrated that Iranian medicinal herbs of the Asteraceae family are generally used to treat and reduce pain. Although the herbs in this family may be considered as alternative agents for pain treatment, further studies are required to clear the accurate anti-nociceptive mechanisms and toxicity of these plants in human subjects.

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Conflict of Interest

The authors declare that they have no conflict of interest.

References

1. Johnson Q, Borsheski R, Reeves-Viets JR. A Review of Management of Acute Pain Mo Med. 2013; 110(1):74–9.
2. Carr DB, Leonidas GC. Acute pain. The Lancet. 1999;353:2051–8.
3. Cohen MJ, Schecter WP. Perioperative pain control: A strategy for management. Surg Clin N Am. 2005:1243–57.
4. Dunckley P, Wise RG, et al. A comparison of visceral and somatic pain processing in the human brainstem using functional magnetic resonance imaging. Journal of Neuroscience. 2005;25(32):7333–41.
5. Hollmann MW, Durieux ME. Local anesthetics and the inflammatory response: A new therapeutic indication. Anesthesiology. 2000;93(3):858–75
6. Ballantine JC, Mao J. (2003). Opioid therapy for chronic pain. N Engl J Med 349:1943–53.
7. Chapman CR, Casey KL, Dubner R, et al. (1985). Pain measurement: An overview. Pain 22:1–31.
8. Foley KM. The treatment of cancer pain. New England Journal of Medicine. 1985;313(2):84-95.
9. Khazir J, Mir BA, Mir SA, et al. Natural products as lead compounds in drug discovery. J Asian Nat Prod Res 2013;15(7):764-88 .
10. Wachtel-Galor S, Benzie IFF. Herbal medicine: an introduction to its history, usage, regulation, current trends, and research needs. In: Benzie IFF, Wachtel-Galor S, editors. Herbal medicine: biomolecular and clinical aspects. 2nd edition. CRC Press; Boca Raton (FL);2011.
11. Mishra BB, Tiwari VK. Natural products in drug discovery: clinical evaluations and investigations. Oppor Chall Scope Nat Prod

Med Chem 2011;1:1-61.
12. Cragg GM, Newman DJ. Natural products: a continuing source of novel drug leads. Biochim Biophys Acta 2013;1(6):3670-95
13. Bessada AMF, Barriera J, Oliviera M. Asteraceae species with most prominent bioactivity and their potential applications: A review. Ind Crops Prod 2015; 76:604-15.
14. Narasimhulu G, Reddy KK, Mohamed J. The genus polygonum (Polygonaceae): an ethnopharmacological and phytochemical perspectives - review. J Pharm Pharm Sci. 2014;6:21-45.
15. Muley B, Khadabadi S, Banarase N. Phytochemical constituents and pharmacological activities of Calendula officinalis Linn (Asteraceae): a review. Trop J Pharm Res. 2009;8:455-465.
16. Golshani S, Karamkhani F, Monsef-Esfehani HR, Abdollahi M. Antinociceptive effects of the essential oil of Dracocephalum kotschyi in the mouse writhing test. J pharm pharm Sci. 2004 Apr 20;7(1):76-9.
17. Eidi A, Oryan S, Zaringhalam J, Rad M. Antinociceptive and anti-inflammatory effects of the aerial parts of Artemisia dracunculus in mice. Pharmaceutical biology. 2016 Mar 3;54(3):549-54.
18. Farahpour MR. Antioxidant activity, Antinociceptive and anti-inflammatory effects of Pot marigold hydroalcoholic extract on experimental animals. Inter. J. Pharm. Tech. Res. 2014;1:974-4304.
19. Sofiabadi M, Azhdari-Zarmehri H, Naderi F, Ghalandari-Shamami M, Sonboli A, Haghparast A. Effects of hydroalcoholic extract of tanacetum sonbolii (Asteraceae) on pain-related behaviors during formalin test in mice. Basic and Clinical Neuroscience. 2014;5(2):162.
20. Maham M, Moslemzadeh H, Jalilzadeh-Amin G. Antinociceptive effect of the essential oil of tarragon (Artemisia dracunculus). Pharmaceutical biology. 2014 Feb 1;52(2):208-12.
21. Zeraati F, Esna-Ashari F, Araghchian M, Emam AH, Rad MV, Seif S, Razaghi K. Evaluation of topical antinociceptive effect of Artemisia absinthium extract in mice and possible mechanisms. African Journal of Pharmacy and Pharmacology. 2014 May 22;8(19):492-6.
22. Fathi M, Hosseinmardi N, Rohampour K, Janahmadi M, Sonboli A, Zaringhalam J. Anti-nociceptive effect of Tanacetum Fisherae on formalin-induced inflammatory pain in rats. Physiology and Pharmacology. 2016;20(3):189-96.
23. Hassanzadeh-Kiabi F, Negahdari B. Antinociceptive synergistic interaction between Achillea millefolium and Origanum vulgare L. extract encapsulated in liposome in rat. Artificial cells, nanomedicine, and biotechnology. 2018;46(5):994-1000.
24. Hadi A, Hossein N, Shirin P, Najmeh N, Abolfazl M. Anti-inflammatory and analgesic activities of Artemisia absinthium and chemical composition of its essential oil. Int J Pharm Sci Rev Res. 2014;38:237-44.
25. Darabian A, Mosavi Z, Asgarpanah J, Bakhtiarian A. In vivo analgesic and anti-inflammatory effects of the essential oil from Artemisia sieberi fruit. Research Journal of Pharmacognosy. 2017;4(4):7-15.
26. Tadayoni Z, Shafaroodi H, Asgarpanah J. Analgesic and Anti-inflammatory activities of the essential oil from Artemisia aucheri boiss. Journal of Essential Oil Bearing Plants. 2018;21(2):440-8.
27. Oryan S, Nasri S, Amin G, Kazemi-Mohammady SM. Anti nociceptive and anti-inflammatory effects of aerial parts of Gundelia tournefortii L. on NMRI male mice. Journal of Shahrekord Uuniversity of Medical Sciences. 2011;12.
28. Fallahzadeh AR, Mohammadi S. An investigation of the antinociceptive and anti-inflammatory effects of hydroalcoholic extract of Inula helenium on male rats. Journal of Babol University of Medical Sciences. 2016;18(12):57-63.
29. Ebrahimi T, Setorki M, Dastanpour N. Antinociceptive effects of Artemisia persica boiss essential oil in male mice using formalin and tail immersion tests. Qom University of Medical Sciences Journal. 2019;12(11):23-31.
30. Asgari A, Parvin N. The analgesic effect of ethanolic extract of Tanacetum parthenium in acetic acid model. Zahedan J Res Med Sci. 2013;15(8):22-5.
31. Kazemzadeh M, Yaghmaei P, Mohammadi S. Analgesic and Anti-inflammatory Effects of Tanacetum balsamita Essential Oil and One of Its Major Constituents (Quercetin) in Male Rats. Clinical Neurology and Neuroscience. 2017;1(3):60-6.
32. Zarei M, Mohammadi S, Komaki A. Antinociceptive activity of Inula britannica L. and patuletin: In vivo and possible mechanisms studies. Journal of ethnopharmacology. 2018;219:351-8.
33. Sayyah M, Hadidi N, Kamalinejad M. Analgesic and anti-inflammatory activity of Lactuca sativa seed extract in rats. J Ethnopharmacol. 2004;92(2-3):325-9.
34. Zarei M, Mohammadi S, Shahidi S, Fallahzadeh AR (2017) Effects of Sonchus asper and apigenin-7-glucoside on nociceptive behaviours in mice. J Pharm Pharmacogn Res;5(4):217-27.
35. Golshani Y, Mohammadi S. Antinociceptive and Acute Toxicity Effects of Erigeron acer L. In Adult Male Rats. J. Med. Plants. 2017;16(62):85-93.
36. Vahidi A, Dashti MH, Jamaladdini SH. Antinociceptive effect of chamomill on formalin induced pain in rat. Sci J Shahid Sadoughi Univ Med Sci Health Ser. 2001;9(2):60-5.
37. Stockwell C. Nature's pharmacy: a history of plants and healing. Random House, London, UK, 1988.
38. World Health Organization. WHO traditional medicine strategy 2014–2023. WHO, Geneva, Switzerland, 2013.
39. World Health Organization. The use of herbal medicine in primary health care. In: Report of the Regional Meeting. 10–12 March 2009, Yangon, Myanmar. WHO, New Delhi. 2009. World Health Organization. In: Adherence to long term therapies: evidence for action. WHO, Geneva, Switzerland, 2003.
40. Karak P. Biological activities of flavonoids: an overview. Int J Pharm Sci & Res. 2019 10(4): 1567-74.
41. Ferraz CR, Carvalho TT, Manchope MF, Artero NA, Rasquel-Oliveira FS, Fattori V, et al. Therapeutic potential of flavonoids in pain and inflammation: mechanisms of action, pre-clinical and clinical data, and pharmaceutical development. Molecules. 2020;25(3):762.
42. Ginwala R, Bhavsar R, Chigbu DI, Jain P, Khan ZK. Potential role of flavonoids in treating chronic inflammatory diseases with a special focus on the anti-inflammatory activity of apigenin. Antioxidants. 2019;8:35. doi: 10.3390/antiox8020035.
43. Verri WA, Vicentini FT, Baracat MM, Georgetti SR, Cardoso D, Cunha TM, et al. Flavonoids as Anti-Inflammatory and Analgesic Drugs: Mechanisms of Action and Perspectives in the Development of Pharmaceutical Forms. In: Rahman A.U., editor. Studies in Natural Products Chemistry. 1st ed. Volume 36. Elsevier; Amsterdam, The Netherlands: 2012. pp. 297–330.
44. Paduch R, Trytek M, Król SK, Kud J, Frant M, Kandefer-Szerszeń M, et al. Biological activity of terpene compounds produced by biotechnological methods. Pharmaceutical Biology. 2016 Jun 2;54(6):1096-107.
45. Martin-Smith M, Khatoon T. Biological activity of the terpenoids and their derivatives. InProgress in Drug Research/Fortschritte der Arzneimittelforschung/Progrès des recherches pharmaceutiques 1963 (pp. 279-346). Birkhäuser Basel.
46. Guimarães AG, Serafini MR, Quintans-Júnior LJ. Terpenes and derivatives as a new perspective for pain treatment: a patent review. Expert opinion on therapeutic patents. 2014;24(3):243-65.