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Mechanism of Action and Phytochemicals of Some Potential Analgesic Agents from Indian Natural Product: A Review

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ABSTRACT: *Analgesics are class of drugs used to treat pain. Pain is sensory and emotional experience which is unpleasant that doesn't related with the actual or potential tissue damage or circumstances which depicts the damage itself. Generally analgesics side effect is peptic ulcer. Indian society, hereditary and traditionally, used natural products as a treatment. Plants produce secondary metabolites to overcome various diseases. Pharmacological effects on natural products are due to the synergism effect and polyvalent activity. This paper aims to review the potential analgesic agents and action of mechanism of phytochemicals from Indian natural products for the further improvement of its utility in curing pain and maintaining good health. Based on this, the pain can be overcome by using various natural products including Aloe Vera (Aloe vera), Papaya (Carica papaya), Noni (Morinda citrifolia), Ginger (Zingiber officinale), Kalmegh (Andrographis paniculata), Betel (Piper betle), and Turmeric (Curcuma longa). In general, the mechanism of the plants to relieve the pain is by suppressing the expression of cyclo-oxygenase (COX-2).*
KEY WORDS: *Analgesics, natural products, pain.*

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I. INTRODUCTION

Pain is one signal of tissue damage due to mechanical, chemical or physical stimulation. Pain perception is supported by neuro-sensory system and afferent nerve lanes, which especially responding to potential harm [1]. Pain which caused by mechanic, chemical, or physic (calor, electricity) stimulus could rise the potential damage to the tissue [2]. It stimulates the release of certain substances called pain mediator such as histamine, bradykinin, leukotrien, and prostaglandin [1]. Those entire pain mediators stimulate pain receptors which channel the stimulation to the brain through the nerves points which has many synapse through spinal cord, marrow advanced, and midbrain. From thalamus impulse stimulus then transferred to the pain center in the large brain, where the impulse is felt as pain. Analgesics are class of drugs used to treat pain. Generally analgesics side effect is peptic ulcer [2].

Plants-based medication has become the tradition and culture in every ethnic in the world especially in India. Plant contains many secondary metabolites which have the important value in pharmacology field and can be used to cure many diseases [3]. Pharmacological effects on natural products due to the synergism effect and polivalent activity [4]. Based on that, the pain can be cured by herbal medications. Plants produced secondary metabolites to overcome various diseases. This paper aims to review the potential analgesic agents and action mechanism of phytochemical from Indian natural products for the further improvement of its utility in curing pain and maintaining good health.

II. RESULT AND DISCUSION

a) Aloe Vera (*Aloe vera*)

Aloe vera contains secondary metabolite such as flavonoids [5], tannin [6,7], saponins, glycoside, alkaloid [8,9] terpenoids, phlobatannin [10,11] and anthraquinone [6]. A group of workers stated that aloe vera extract which has a function as anti-arthritis [12] is anthraquinone while another group stated that aloe vera contain of lupeol and salicylic acid which are the effective compounds as pain reliever [13].

Ethanol and methanol extract from aloe vera are proven to have activities that can relieve the pain. It has been proven through the in vitro study which shows that the extract, could potentially suppress the expression of cyclo-oxygenase (COX-2) [14], as one of the way the NSAID medicine works. It has also been proven through in vivo where ethanol and methanol could significantly increase the analgesic effect when it is injected to rats [15]. The analgesic activity is derived from the existence of carboxypeptidase and bradikinase enzyme which function is to lessen or to relieve the pain. The reduction of pain happens when immune system is stimulated and blocked the biosynthesis prostaglandin [14] which is responsible for the occurrence of pain [10,16].

According to another research, 300mg/kg dose of aloe vera infusion is effective as analgesic for somatic pain and for internal body pain without any side effects for kidneys and liver [1].

b) Papaya (*Carica papaya*)

Papaya leaves contain vitamin E, glycoside, alkaloid, saponin, carposid, sucrose, dextrose, levulosa, papain enzyme, pseudocarpain [17], steroid, quinone, anthraquinone, [18], tannin [19] and flavanoid [20]. Papain and chymopapain are the strong component to be the active compounds which produce analgesic effect to the extract of papaya's leaves [18].

Papaya leaves has been proven to have analgesic activity [21]. It is caused by ethanol extract of papaya leaves contain of flavanoid which has been known could block inflammatory formation that causes the pain. Flavanoid blocks cyclooxygenase I (COX I) which has a role in prostaglandin biosynthesis as pain formation mediator, so that it will blocks the occurrence of pain [19]. Papaya leaves also has papain enzyme which has analgesic activity. Methanol extract of Papaya seeds also had been proven could lessen the pain with possible mechanism which inhabiting pain mediator such as histamine, prostaglandin, and sitokin [21-23].

c) Noni (*Morinda citrifolia*)

Noni fruits contain 90% water and other crucial substances such as glutamate acid, aspartat acid, isoleusin, fenol substances (scopoletin, proxeronine, xeronine, morindone rubiadin), anthraquinone [24], askorbat acid, pro-vitamin A [25], alkaloid, and terpenoid [26]. There are also other substances in Noni which expected to have analgesic quality such as proxeronine and xeronine.

The extract of Noni shows the significant analgesic effect when it was given to the mice. The administration and 2 of Noni's juice to mice has increasing mice's tolerance to the pain. The extract of Noni is expected to block histamine and prostaglandin receptors hich are the receptors of pain. Noni's ethanol extract has better analgesic effect than paracetamol to the mice [24]. Besides, it has been proven that 75% of aqueous extract of noni's roots had the same potency as morphine. On that dose it doesn't causes addiction effect, side effects [26], and toxic effects [24]. A group of scientists proved that the aqueous extract of Noni's seeds 8 mg/kg dose has shown a significant analgesic effects [27].

d) Ginger (*Zingiber officinale*)

The content of secondary metabolite on ginger rhiz ome are alkaloid, flavanoid, saponin, tanin, terpenoid, steroid [28], gingiberin (20,57%), beta seiqufelandrin (12,71%), kurkumin (11,27%), gingerol (4,46%), shogaol, paradol, gingerdione [29,30]. Gingerol and Shargaol are the compounds which responsible for analgesic activity on ginger rhizome [31].

Ginger has been proven could inhibit prostaglandin biosynthesis which has the same mechanism as Non-Steroidal Anti-Inflammatory Drugs (NSAID) [29]. Based on the result of in vitro study, ginger rhizome and its main compounds such as gingerol and shargaol could block COX enzyme synthesis and pain mediator synthesis such as prostaglandin and leukotrin [31,32]. Based on research, it is listed from the one which has the highest effect on its content to block the COX-2 enzyme synthesis is paradol, shogaol, gingerol and gingerdione. Another research work has proved that ginger rhizome has an effect to several genes which encoding sitokin, kemokin and COX-2 enzyme [33].

e) Kalmegh (*Andrographis paniculata*)

A review of the literature reveals that the presence of various chemical constituents in the aerial parts of the *Andrographis paniculata* are andrographolide, which is diterpene lactone, colourless, crystalline, bitter in taste [34]. Other compounds include 14-deoxy-11-oxoandrographolide, didehydro andrographolide /andrographlide D, 14-deoxy-andrographolide, non-bitter compound is neo andrographolide, homoandrographolide, andrographosterin, andrograpanin, α-sitosterol, stigmasterol. Apigenin-7, 4-dio-methyl ether, 5- hydroxy 7,8,2, 3-tetramethoxy flavones, monohydroxy trimethyl flavones, andrographin, dihydroxy di-methoxy flavoue, panicolin, andrographoneo, andrographoside, andropani-culoside, andrograpanin, Isoandrographolide and skollcaflavone. Six entlabdane diterpenoids i.e. 3-o-beta-Dglucopyranosyl-14, 19- di-deoxy-andrographolide, 14-deox, 17- hydroxyl andrographolide, 19-o-[beta-D-apiofuranosy 1-2beta- D-glucopyranoyl]-3, 14-dideoxyandiographolide, 3-obeta-Dglucopyranosyl- andro-grapholide, 12S-hydroxy andrographolide and andrographatoside. These compounds showed inhibitor activity against several fungal and bacterial strains. Dua *et al*. reported four xanthones 1,8-di hydroxyl 3,7- dimethoxy xanthone, 4,8-di-hydroxy-2, 7- dimethoxyxanthones, 1,2-dihydroxy-6, 8-di methoxy xanthone and 3,7,8-trimethoxy-1-hydroxyxanthone from the roots [35,36].

Andrographolide is the main active component of these plants [37]. Androghapolide which is being isolated from Bitter leaves is responsible to the analgesic activities of that plant. Andrographolide which is being isolated from extract Kalmegh leaves has been proven to have significant analgesic activity on 300mg/kg dose.

Its mechanism is by reducing the expression process of COX-2 and reducing the expression gene of COX-1 [38], and also releasing the pain mediator histamine [34].

f) Betel (Piper Betle)

The compounds in Betel leaves are alkaloid, tanin [39], alipirokatekol, kavibetol, eugenol, dan safrol [40]. The active compound which responsible for analgesic activity of betel leaves is eugenol [40]. The methanol extract of betel has been proven to have significant analgesic activities even though the result is not as good as narcotic analgesic [41], the analgesic activity is significantly shown that it could decrease the histamine production [42,43], it is also shown that its mechanism works in the central of pain receptor which is in the center of nerve system [44]. Eugenol's analgesic activities stated to have mechanisms as gene suppression and its function is to express siklooksigenase-2 enzyme (COX-2) [40].

g) Turmeric (*Curcuma longa*)

The compounds in turmeric rhizome are curcumin [45], flavanoid, glikoside, phenol [46], alkaloid, saponin, tannin [47], phlobatanin, antosianin [48]. The active components which responsible for turmeric analgesic activity is curcumin [49,50]. The research done by [51], found that curcumin gave significant analgesic effect when it was examined to the rats. Curcumin reported to work by suppressing siklooksigenase-2 (COX-2) enzyme production which responsible for prostaglandin sinthesis process [52], it even be said that curcumin can relieve the pain with the same mechanism as NSAID [45]. The research done by [53], curcumin has been proven to decrease siklooksigenase-2 (COX-2) level on mice. Curcumin has also been proven can lessen the pain in neuropathic disease by inhibiting CBP Histone acetyltransferase which function to regulate the expression of COX-2 on mice [49]. The research done by [54], showed the significant analgesic activity was proven by Tail-flick method on albino rat. Turmeric leaves has also been proven could lessen the pain caused by chronic pain which occur in rheumatoid arthritis disease or cancer [47].

III. CONCLUSION

Pain can be overcome by using natural products including Aloe Vera (*Aloe vera*), Papaya (*Carica papaya*), Noni (*Morinda citrifolia*), Ginger (*Zingiber officinale*), Kalmegh (*Andrographis paniculata*), Betel (*Piper betle*), and Turmeric (*Curcuma longa*). The general mechanism of the plants to relieve the pain is by suppressing the expression of cyclo-oxygenase (COX-2).

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REFERENCES

[1] Ghosh, A.K., M. Banerjee, T.K. Mandal, A. Mishra, and M.K. Bhowmik. (2011). A Study on Analgesic Efficacy and Adverse Effects of Aloe vera in Wistar Rats. Pharmacologyonline 1: 1098-1108.

[2] Nalamachu, S. (2013). An Overview of Pain Management: The Clinical Efficacy and Value of Treatment. American Journal Manag Care19 (16): 261-266.

[3] Mans, Dennis R. A. (2013). From Forest to Pharmacy: Plant Based Traditional Medicines as Sources for Novel Therapeutic Compounds. Academia Journal of Medicinal Plants 1(6):101-110.

[4] Bone, K., and Mills, S., (2013). Principles and Practice of Phytotherapy, Second Edition, Churchill Livingstone Elsevier, New York.

[5] Mariappan, V., and G. Shanthi. (2012). Antimicrobial and Phytochemical Analysis of Aloe vera L. International Research Journal of Pharmacy 3 (10): 158-161.

[6] Kumar, H.N.K., E. Chandana, S.D. Preethi, and J.B. Chauhan. (2012). In Vitro Antimicrobial Activity and Phytochemical Screening of Aloe vera Linn. International Journal of Current Pharmaceutical Research 4 (3): 45-47.

[7] Raphael, E. (2012). Phytochemical Constituents of some Leaves extract of Aloe vera and Azadirachta indica Plant Species. Global Advanced Research Journal of Environmental Science and Toxicology 1 (2): 14-17.

[8] Yebpella, G.G., H.M.M. Adeyemi, C. Hammuel, A.M. Magomya, A.S. Agbaji, and E.M. Okonkwo. (2013). Phtochemical Screening and Comparative Study of Antimicrobial Activity of Aloe vera Various Extracts. African Journal of Microbiology Research 5 (10): 1182- 1187.

[9] Thu, K., Y.Y. Mon, T.A. Khaing, and O.M. Tun. (2013). Study on Phytochemical Properties, Antibacterial Activity and Cytotoxicity of Aloe vera L. World Academy of Science, Engineering and Technology 7 (5): 114-118.

[10] Devaraj, A., and T. Karpagam. (2011). Evaluation of Anti-inflammatory Activity and Analgesic Effect of Aloe vera Leaf Extract in Rats. International Research Journal of Pharmacy 2 (3): 103-110.

[11] Karpagam, T., and R.A. Devaraj. (2011). Studies on the Efficacy of Aloe vera on Antimicrobial Activity. International Journal of Research in Ayurveda and Pharmacy 2 (4): 1286-1289.

[12] Kaur A., P. Nain, and J. Nain. (2012). Herbal Plants Used in Treatment of Rheumatoid Arthritis: A Review. International Journal of Pharmacy and Pharmaceutical Sciences 4 (4): 44-57.

[13] Rajeswari, R., M. Umadevi, C.S. Rahale, R. Puspha, S. Selvavenkadesh, K.P.S. Kumar, and D. Bhowmik. (2012). Aloe vera : The Miracle Plants Its Medicinal and Traditional Uses in India. Journal of Pharmacognosy and Phytochemistry 1 (4): 118-124.

[14] Shahraki, M.R., H. Mirshekari, and A. Sabri. (2014). Aloe vera Aqueos Extract on Morphine Withdrawal Syndrome in Morphine-Dependent Female Rats. International Journal High risk Behaviour Addict 3 (3): 1-4.

[15] Cowan, D. (2007). Oral Aloe vera as a Treatment for Osteoarthritis: a Summary. British Journal of Community Nursing 5 (6): 280-282.
[16] Egesie, U.G., K.E. Chima, and N.Z. Galam. (2011). Anti-inflammatory and Analgesic Effects of Aqueous Extract of Aloe vera (Aloe barbadensis) in Rats. African Journal Biomed Research 14: 209-212.
[17] Hasimun P., Suwendar, and G.I. Ernasari. (2014). Analgetic Activity of Papaya (Carica papaya) Leaves Extract. Procedia Chemistry 13: 147-149.
[18] Owoyele, B.V., O.M. Adebukola, A.A. Funmilayo, and A.O. Soladoye. (2008). Anti-Inflammatory Activities of ethanolic Extract of Carica papaya Leaves. Inflammopharmacology 16: 168-173.
[19] Alex, A., A. Eguonor, V. Eguonor, and Orhehe. (2013). Antinociceptive and Anti-Inflammatory Studies of the Aqueous Leaf Extract of Carica papaya in Laboratory Animals. Asian Journal Exp. Biological Science 4 (1): 89-96.
[20] Imaga, N.A., G.O. Gbenie, V.I. Okochi, S. Adenekan, T.D. Emmanuel. B. Oyeniyi, P.N. Dokai, M. Oyenuga, A. Otumara, and F.C. Ekeh. (2010). Phytochemical and Antioxidant Nutrient Constituents of Carica papaya and Parquetina nigrescens Extracts. Scientific Research and Essays 5 (16): 2201-2205.
[21] Amazu, L.U., C.C.A., Azikiwe, C.J. Njoku, F.N., Osula, P.J.C., Nwosu, A.O., Ajugwo, and J.C. Enye. (2010). Antiinflammatory Activity of the Methanolic Extract of the Seeds of Carica papaya in Experimental Animals. Asian Pacific Journal of Tropical Medicine: 884-886.
[22] Anaga, A.O., and E.V. Onehi. (2010). Antinociceptive and Anti-inflammatory Effects of the Methanol Seed Extract of Carica papaya in Mice and Rats. African Journal of Pharmacy and Pharmacology 4 (4) : 140-144.
[23] Tamma, N.K., T.D. Ashraf, L. Nagakrishna, L. Sudhakar, and S. Challa. (2013). Evaluation of Antinociceptive and Anti-Inflammatory Effect of Aqueos Seed Extract of Carica papaya Linn in Albino Rats. Internationa Journal of Medical and Helath Sciences 2 (3): 305-310.
[24] Blanco, Y.C., F. Vaillant, A.M. Perez, M. Reynes, J.M. Brillouet, and P. Brat. (2006). The Noni Fruit (Morinda citrifolia L.): A review of Agricultural Research, Nutritional and Therapeutic Properties. Journal of Food and Analysis 19: 645-654.
[25] Singh, R.D. (2012). Morinda citrifolia L. (Noni): A Review of the Scientific Validation for its Nutritional and Therapeutic Properties. Journal of Diabetes and Endocrinology 3 (6): 77-91.
[26] Wang, M.Y., B.J. West, C.J. Jensen, D. Nowicki, C. Su, A.K. Palu, and G. Anderson. (2002). Morinda citrifolia (Noni) : A Literature Review and Recent Advances in Noni Research. Acta Pharmacologica Sinica 12: 1127-1141.
[27] Younos, C., A. Rolland, J. Fleurentin, M.C. Lanhers, R. Misslin, and F. Mortier. (1990). Analgesic and Bhavioural Effects of Morinda citrifolia. Planta Med 56: 430-435.
[28] Anosike, C.A., O. Obidoa, U.S. Lawrence, Ezeanyika and M.M. Nwuba. (2009). Anti-inflammatory and Anti-ulcerogenic Activity of the Ethanol Extract of Ginger (Zingiber officinale). African Journal of Biochemistry Research 3 (12): 379-384.
[29] Bhargava, S., K. Dhabhai, A. Batra, A. Sharma, and B. Malhotra. (2012). Zingiber officinale : Chemical and Phytochemical Screening and Evaluation of its Antimicrobial Activities. Journal of Chemical and Pharmaceutical Research 4 (1): 360-364.
[30] Hasan, H.A., A.M.R. Raauf, B.M.A. Razik, and B.A.R. Hassan. (2012). Chemical Composition and Antrimicrobial Activity of the Crude Extracts Isolated from Zingiber officinale by Different Solvents. Pharmaceutica Analytica Acta 3 (9): 1-5.
[31] Mahluji, S., A. Ostadrahimi, M. Mobasseri, V.E. Attari, and L. Payahoo. (2013). Anti-Inflammatory Effects of Zingiber officinale in Type 2 Diabetic Patients. Advanced Pharmaceutical Bulletin 3 (2): 273-276.
[32] Awed, H., T. El-saidy, and T. Amro. (2013). The Use of Fresh Ginger Herbs as a Home Remedy to Relieve Primary Dysmenorrhea. Journal of Research in Nursing and Midwifery 2 (8): 104-113.
[33] Charlier C., and C. Michaux. (2003). Dual Inhibition of Cyclooxygenase-2 (COX-2) and 5-Lipoxygenase (5-LOX) as a New Strategy to Provide Safer Non-Steroidal Anti-inflammatory Drugs. European Journal of Medicinal Chemistry 38: 645-659.
[34] Niranjan, A., S.K., Tewari, and A. Lehri. (2010). Biological Activities of Kalmegh (Andrographis paniculata Nees) and its Active Principle- A Review. Indian Journal of Natural Products and Resources 1 (2): 125-135.
[35] Dua, V.K., Ojha, V.P., Roy, R., Joshi, B.C., Valecha, N., and Devi, C.U. (2004). Anti-malarial activity of some xanthones isolated from the roots of Andrographis paniculata, Journal of Ethnopharmacology 95:247-251.
[36] Nyeem, M. A. B., Mannan, M.A., Nuruzzaman, M., Kamrujjaman, K. M. and Das, S. K. (2017). Indigenous king of bitter (Andrographis paniculata): A review. Journal of Medicinal Plants Studies 5(2): 318-324.
[37] Benoy, G.K., D.K. Animesh, M. Aninda, D.K. Priyanka, and H. Sandip. (2012). An Overviw on Andrographis paniculata (Burm. F.) Nees. IJRAP 3 (6): 752-758.
[38] Lim, J.C.W., T.K. Chan, S.W. Ng. David, S.R. Sagineedu, J. Stanslas, and W.S.F. Wong. (2012). Andrographolide and Its Analogues : Versatile Bioactive Molecules for Combating Inflammation and Cancer. Clinical and Experimental Pharmacology and Physiology 39: 300-310.
[39] Pradhan, D., K.A. Suri, D.K. Pradhan, and P. Biswasroy. (2013). Golden Heart of the Nature : Piper betle L. Journal of Pharmacognosy and Phytochemistry 1 (6): 147-167.
[40] Bhalerao, S.A., D.R. Verma, R.V. Gavankar, N.C. Teli, Y.Y. Rane, V.S. Didwana, and A. Trikannad. (2013). Phytochemistry, Pharmacological Profile and Therapeutic Uses of Piper betle Linn. – An Overview. Research and Reviews: Journal of Pharmacognosy and Phytochemistry 1 (2): 10-19.
[41] Alam, Md.B., F. Akter, N. Parvin, R.S. Pia, S. Akter, J. Chowdhury, K.S. E-Jahan, and Md.E. Haque. (2012). Antioxidant, Analgesic, and Anti-Inflammatory Activities of the Methanolic Extract of Piper betle Leaves. Avicenna Journal of Phytomedicine : 1-14.
[42] Kumar, N., P. Misra, A. Dube, S. Bhattacharya, M. Dikshit, and S. Ranade. (2010). Piper betle Linn. A Meligned Pan-Asiatic Plant with an Array of Pharmacological Activities and Prospects for Drug Discovery. Current Science 99 (7): 922-932.
[43] Dwivedi, V. and S. Tripathi. (2014). Review Study on Potential Activity of Piper betle. Journal of Pharmacognosy and Phytochemistry 3 (4): 93-98.
[44] Datta, A., S.V. Bhalerao, P.P. Shidore, A.V. Tilak, S. Patil, and T. Desphande. (2014). To Evaluate the Analgesic Efficacy of an Ethanolic Extract of Piper betle Linn. (paan) and Its Probable Mechanism of Action Using Animal Models. Research Journal of Pharmaceutical, Biological, and Chemical Sciences 5 (3): 424-431.
[45] Kapoor, S. (2012). Curcumin and Its Emerging Role in Pain Modulation and Pain Management. The Korean Journal of Pain 25 (3): 202-203.
[46] Arutselvi, R., T. Balasaravanan, P. Ponmurugan, N.M. Saranji, and P. Suresh. (2012). Phytochemical Screening and Comparative Study of Anti Microbial Activity of Leaves and Rhizomes of Turmeric Varieties. Asian Journal of Plant Science and Research 2 (2) : 212-219.

[47] Hasan, M.N., A. Ferdoushi, N. Ara, S. Rahman, Md.S. Hossan, and M. Rahmatullah. (2014). Preliminary Phytochemical Screening, Toxicity, Antihyperglycemic and Analgesic Activity Studies with Curcuma longa Leaves. World Journal of Pharmacy and Pharmaceutical Sciences 3 (9): 81-91.
[48] Sawant, R.S., and A.G. Godghate. (2013). Qualitative Phytochemical Screening of Rhizomes of Curcuma longa Linn. International Journal of Science, Environment 2 (4): 634-641.
[49] Zhu, X., Q. Li, R. Chang, D. Yang, Z. Song, Q. Guo, and C. Huang. (2013). Curcumin Alleviates Neuropathic Pain by Inhibiting p300/CBP Histone Acetyltransferase Activity-Regulated Expression of BDNF and COX-2 in a Rat Model. PLOS ONE 9 (3): 1-9.
[50] Ikawati, Z., N. Yulianti, and S.A. Margono. (2014). The Analgesic Effect of a Curcumin Analogue 1,5-bis(4'hydroxy-3'-methoxyphenyl)-1,4-pentadien-3-on (Gamavuton-0) in Acute and Persistent Pain. Journal of Applied Pharmaceutical Science 4 (8): 48-51.
[51] Haider, S., F. Naqvi, S. Tabassum, S. Saleem, Z. Batool, S. Sadir, S. Rasheed, D. Saleem, A. Nawaz, and S. Ahmad. (2013). Preventive Effects of Curcumin Againts Drug- and Starvation-Induced Gastric Erosions in Rats. Scientia Pharmaceutica 81: 549-558.
[52] Jung, K.T., and K.J. Lim. (2014). Curcumin, COX-2, and Protein p 300/CBP. The Korean Journal of Pain 27 (4): 365-366.
[53] Zanjani, T.M., H. Ameli, F. Labibi, K. Sedaghat, and M. Sabetkasaei. (2014). The Attenuation of Pain Behavior and Serum COX-2 Concentration by Curcumin in a Rat Model of Neuropathic Pain. The Korean Journal of Pain 27 (3): 246-252.
[54] Sundarananthavalli, S., A. Kulandaisamy, and C.C. Christopher. (2011). Synthesis, Characterisation, Analgesic, Anti-Inflammatory, Anti-Ulcer, Woundh Healing and Antimicrobial Effects of Curcuminoids. International Journal of Chem Tech Research 3 (4): 20140-2046.

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