ฤทธิ์ต้านอักเสบของสำมะงา

The anti-inflammatory effects of *Clerodendrum inerme*

ศรินรัตน์ ฉัตรธีระนันท์
Sarinrut Chattiranan
สาขาวิชาเคมี คณะวิทยาศาสตร์และเทคโนโลยี มหาวิทยาลัยราชภัฏเพชรบุรี
Division of Chemistry, Faculty of Science and Technology, PhetchaburiRajabhat University, Phetchaburi, Thailand

บทคัดย่อ

การค้นหาตัวยาต้านอักเสบชนิดใหม่ๆ ที่มีความเป็นพิษต่ำเป็นสิ่งที่ได้รับความสนใจเป็นอย่างมากในการพัฒนายา สำมะงาเป็นพืชในสกุล *Clerodendrum* ที่น่าใจเป็นอย่างยิ่งเพราะมีองค์ประกอบทางเคมีหลายชนิดที่มีฤทธิ์ต้านอักเสบ สารออกฤทธิ์ที่สำคัญได้แก่ ลูทีโอลิน เวอร์บาสโคไซด์ และเอพิเจนิน โดยสารเหล่านี้แสดงฤทธิ์ต้านอักเสบอย่างแรง บทความนี้นำเสนอเนื้อหาเกี่ยวกับการศึกษาฤทธิ์ต้านอักเสบและองค์ประกอบทางเคมีของสำมะงาที่แสดงฤทธิ์ต้านอักเสบเพื่อนำไปสู่การนำพืชที่มีคุณค่าชนิดนี้ไปใช้ประโยชน์ต่อไป

คำสำคัญ : ฤทธิ์ต้านอักเสบ สำมะงา

Abstract

The searching of novel effective anti-inflammatory compounds with low toxicity is among the most interesting in drug development. The plant *Clerodendrum inerme* (L.) belongs to the genus *Clerodendrum* and possess several active ingredients for anti-inflammatory approaches. The major active compounds such as luteolin, verbascoside and apigenin have made this plant intriguing because of their strong anti-inflammatory activities. This review covers the anti-inflammatory activities of compounds found in *Clerodendrum inerme* (L.), which may facilitate in dept investigations into the use of this valuable plant.

Keywords: anti-inflammatory effect, *Clerodendrum inerme*

Introduction

Inflammation is the mechanism of body response to heal the damaged cells as well as tissues caused by injuries like physical trauma, pathogens, toxic chemical and microbial agents. Inflammation can be divided into acute and chronic inflammation. The acute inflammation begins within the first few hours or days following the injury of tissues inwhich three main processes occur: increased blood flow, increased permeability and migration of leukocytes, such as neutrophils. The classical signs of acute inflammation are pain, heat, redness, swelling, and loss of motor function. If the condition causing acute inflammation is not resolved, the inflammation may transform into a longer term chronic inflammation, which leads to onset of diseases [1]. Nowadays, the need for

Corresponding author. E-mail address : kae_2028@hotmail.com

anti-inflammation drugs including Non-steroidalanti-inflammatory drugs (NSAIDS), such as Aspirin, Celecoxib, Dichlofenac, Inuprofen and Indomethacin continuously increases. The fact that in certain conditions such drugs can produce gastrointertinal irritation and renal damage [2] has led to the avoidance of use. In the line of pharmacological researches, the novel anti-inflammatory actives derived from natural products are among the most interesting. The compounds obtained from plants are generally acceptable by the patients because of their reputation for safety.

Focusing on the genus *Clerodendrum*, more than five hundred species have been identified like shrubs, herbs and small trees that are widely distributed in Asia, Australia, Africa and America [3].This genus is being used as ethnomedicines for the treatment of diabetes mellitus [4], anti-inflammatory [5], antimicrobial [6-7], anti-malarial activities [8] and anticancer [9]. In addition, the major secondary metabolites have been reported, including terpenoids, neo-clerodanediterpenes, sterols, iridoids and phenolic compounds. In case of phenolic compound, phenyl propanoids and flavonoids are found as a predominant class. In addition, macrocyclic alkaloids and cyanogenic glycosides are found in a few species [10].This review mainly covers the anti-inflammatory activities of *Clerodendrum inerme* (L.)

Anti-inflammatory effects of *C. inerme*

Clerodendrum inerme (L.) Gaertn, locally called “Samma nga”, is a shrub that could reach up to 2 m tall. The ovate leaves are opposite. The inflorescence is umbel with 3-7 flowers joined at a common base point. The corolla is white, fused with 5 lobes. There are four the stamens, reddish to purple color as showed in Figure 1. *C. inerme* which grows well along the beach is distributed in South, South-east Asia and Pacific islands. It can tolerate the salt of the ocean and is valued as groundcover plant. [11]

Figure 1. *Clerodenrum inerme* [12]

For pharmacological approaches, the roots, stems and fresh and dried leaves of the plant are traditionally used for the treatment of skin disease, local pain, inflammation, asthma, tropical burns and rheumatism [13].

Previous studies also provide the scientific proof that the plant may be useful for the attenuation of inflammation. The methanol extracts of the leaves (0.25%, 0.5%, 1.0%) were previously tested for anti-inflammation by cotton pellet-induced granuloma model in albino rats. The results were found that the extracts inhibited granulatory phases of inflammation in a dose related manner. In addition, the extracts (125, 250, 500 mg/kg) reduced significantly the acetic acid-induced writhing in mice with a dose dependent manner [14]. Furthermore,

the ethanolic extract of whole plants of C. *inerme* was tested for the analgesic and anti-inflammatory activities. The study evaluated the analgesic activities using acetic acid-induced writhing and heat-induced pain in mice. For anti-inflammation, the xylene-induced ear edema mice model revealed that at the doses of 250 and 500 mg/kg body weight, the ethanolic extract of C. *inerme* significantly inhibited the acetic acid-induced writhing by 26.39% and 45.83%, respectively, comparing to 57.64% inhibition of the standard analgesic drug, dilodenac sodium. Heat-induced pain in mice showed the significant analgesic activity of the extract at the doses of 500 mg/kg body weight and the effect of the C. *inerme* extract was comparable to that of Pentazocine. In addition, using Xylene-induced acute ear edema in mice as a model, the extract at the dose of 500 mg/kg body weight showed significant inhibition effect of 29.54%, in comparison to 29.40% of Diclofenace sodium [15].

Not only do the extracts of C. *inerme* exhibit potential anti-inflammatory effects as mentioned above, but also certain compounds found in C. *inerme* were shown to have strong anti-inflammatory activities. It is beneficial to describe herein the anti-inflammation activities of compounds which are compositions of C. *inerme*. The phytochemical constituents of the plant have been identified and the results showed that C. *inerme* composed of steroidal glycoside, megastinmane glucosideds, iridoid glucosides, clerodane glycosides and flavonoids [16-18].

Several pure compounds like luteolin, verbascoside, isoverbascoside, leucosceptoside A, decaffeoylverbascoside, darendoside B, darendoside B, monomelittoside, melittoside, and apigenin have been identified [19]. Among of them, some active compounds like luteolin, verbascoside and apigenin were proved either *in vivo* and *in vitro* to have a potential anti-inflammation. Their active chemical structures are shown in Figure 2.

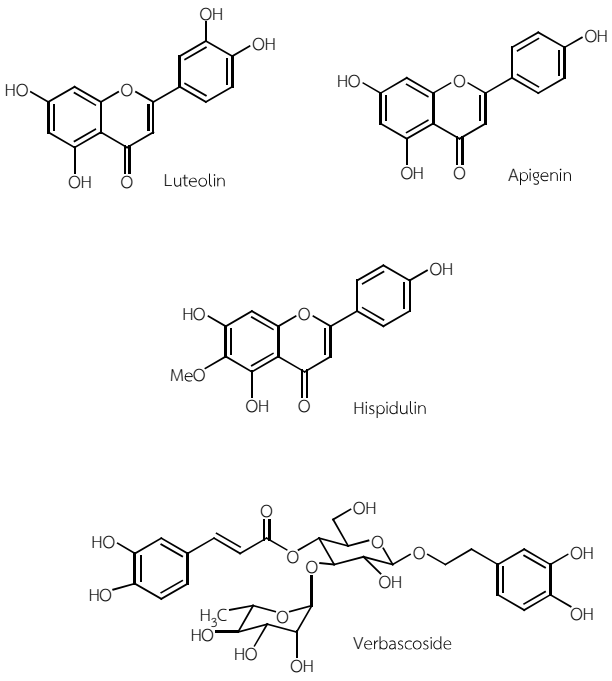

Figure 2. Some anti-inflammatory constituents of *C. inerme*

Luteolin a pure compound found in the C. *inerme* was previously shown to exhibit potent anti-inflammatory effects *in vitro*. The compound was shown to inhibit LPS-induced high mobility group B-1 (HMGB1) secretion and LSP-mediated tumor necrosis factor alpha (TNF-α) in the macrophage cell model [20].

Another compound component of C. *inerme*, verbascoside was shown to have anti-inflammation assessed by arachidonic acid-mediated ear edema in mice [21]. It is worthy to note that verbacoside also exhibits analgesic, antimicrobial and immunosuppressive [22]. Likewise, the compound apigenin was shown to inhibit the collagenase activity associated with the progression of rheumatoid arthritis. Apigenin was shown to suppress LPS-induced nitric oxide (NO) production in macrophage RAW 264.7 cells. In addition, the expression of an inflammatory mediator like cyclooxygenase-2 (COX-2) in LSP-treated macrophages was attenuated by the treatment with apigenin [23]. In recently, the inhibition of NO production guided to isolate three known flavone compounds including acacetin, hispidulin and diosmetin from the ethyl acetate extract of *C. inerme* leaves. All of compounds hispidulin showed the most NO inhibitory effect and also inhibited prostaglandin E_2 (PGE_2) [24]. Reactive oxygen species (ROS) have been long shown to worsen the condition of inflammation and tissue destruction. The presence of high contents of phenolic compounds and flavonoids in this plant may result in antioxidant, as well as radical scavenging activities that may compromise the inflammatory reaction.

Conclusion

As a potential plant possessing anti-inflammatory effect, C. *inerme* and its active components including luteolin, verbascoside apigenin and hispidulin have been scientific proofed both *in vitro* and *in vivo* to be a potential to be used for the suppression of inflammatory process. Furthermore, the long period of use of this plant in traditional means supports the safety of this herbal medicine. This review may provide information necessary to highlight and encourage further investigations to assure the efficacy as well as the safety of use of C. *inerme* for anti-inflammatory approaches.

References

1. Serhan, C., Ward, P. and Gilroy, D.W. 2010. *Fundamentals of inflammation*. New York: Cambridge university.
2. Howland, R.D. and Mycek, M.J. 2006. *Lippincott's illustrated reviews: pharmacology*. 3rd ed. London: Lippincott Williams & Wilkins publishers.
3. Shirivastava, N. and Patel, T. 2007. *Clerodendrum* and healthcare: an overview. *MAPSB*. 1: 142-147.
4. Adeneye, A.A., Adeleke, T.I. and Adeneye, A.K. 2008. Hypoglycemic and hypolipidemic effects of the aqueous fresh leaves extract of *Clerodendrum captatum* in Wistar rats. *J. Ethnopharmacol*. 116: 7-10.
5. Liu, H., Wang, L. and Wang, M.H. 2011. Antioxidant and nitric oxide release inhibition activities of methanolic extract from *Clerodendrum cyrtophyllum* Turcz. *Hort. Environ. Biotechnol*. 52: 309-314.
6. Abbaszadeh, G., Srivastavs, C. and Walia, S. 2014. Insecticidal and antifeedant activities of clerodane diterpenoids isolated from the Indian bhant tree, *Clerodendron infortunatum*, against the cotton bollworm, *Helicoverpa armigera*. *J. Insect Sci*. 14: 1-8.
7. Radha, P.M., Kumar, H., Padmaja, V., Mathew, A. and Kumar A. 2012. Preliminary phytochemical, antimicrobial and toxicity studies on *Clerodendrum paniculatum* Linn leaves. *Hygein. J. D. Med*. 4: 41-50.

8. Deressa, T., Mekonnen, Y. and Animut, A. 2010. In vivo anti-malarial activities of *Clerodendrum myricoides*, *Dodonea angustifolia* and Aloe debrana against *Plasmodium berghei*. *Ethiop. J. Health Dev*. 24: 25-29.
9. Thalla, S., Tammu, J., Pentela, B. and Thalla, S.R. 2012. Evaluation of anticancer activity of *Clerodendrum serratum*. *IJCPS*. 3: 56-60.
10. Patel, J., Acharya, S.R. and Acharya, N. 2014. *Clerodendrum serratum* (L.) Moon. A review on traditional uses, phytochemistry and pharmacological activities. *J. Ethnopharmacol*. 154: 268-285.
11. Chethana, G.S., Hari Venkatesh, K.R. and Gopinath, S.M. 2013. Review on *Clerodendrum inerme*. *JPSI*. 2: 38-40.
12. *Clerodendrum inerme*. [online] available: http://luirig.altervista.org/naturaitaliana/viewpics.php?title=Clerodendrum+inerme. 2014
13. Florence, A.R., Joseph, J. and Jeeva, S. 2012. Intra-specific variation of bioactive principles in select members of the genus Cleodendrum L. *J. Chem. Pharm. Res*. 4: 4908-4914.
14. Yankanchi, S.R. and Koli, S.A. 2010. Anti-inflammatory and analgesic activity of mature leaves methanol extract of Clerodendrum inerme L. (Gaertn). *J. Pharm. Sci. & Res*. 2: 782-785
15. Khanam, D., Deb, D., Dev, S., Shahriar, M., Das, A.K. and Kawsar, H. 2014. Analgesic and anti-inflammatory activities of ethanolic extract of *Clerodendrum inerme* (L.) Gaertn. *BPJ*. 17: 62-66.
16 .Rehman, A.U., Begum, S., Saied, S., Choudhary, M.I. and Akhtar, F. 1997. A steroidal glycoside from *Clerodendrum inerme. Phytochemistry*. 45: 1721-1722.
17. Pandey, R., Verma, R.K. and Gupta, M.M. 2005. Neo-clerodane diterpenoids from *Clerodendrum inerme. Phytochemistry*. 66: 643-648.
18. Kanchanapoom, T., Kasai, R., Chumsri, P. and Hiraga, Y. 2001. Megastigmane and iridoid glucosides from *Clerodendrum inerme*. *Phytochemistry*. 58: 333-336.
19. Shirivastava, N. and Patel, T. 2007. *Clerodendrum* and healthcare: an overview part II phytochemistry and biotechnology. *MAPSB*. 1: 209-233.
20. Chen, D., Bi, A., Dong, X., Jiang, Y., Rui, B., Liu, J., Yin, Z. and Luo, L. 2014. Luteolin exhibits anti-inflammatory effects by blocking the activity of heat shock protein 90 in macrophages. *Biochem. Biophys. Res. Commun*. 443: 326-332.
21. Murai, M., Tamayama, Y. and Nishibe, S. 1995. Phenylethanoids in the herb of *Plantago lanceolata* and inhibitory effect on arachidonic acid-induced mouse ear edema. *Planta Med*. 61: 479-480.
22. Herbert, J.M., Maffrand, J.P., Taoubi, K., Augereau, J.M., Fouraste, I. and Gleye, J. 1991. Verbascodise isolated from *Lantana camara*, an inhibitor of protein kinase C. *J. Nat. Prod*. 54: 1595-1600.
23. Lee, J.H., Zhou, H.Y., Cho, S.Y., Kim, Y.S., Lee, Y.S. and Jeong, C.S. 2007. Anti-inflammatory mechanisms of apigenin: inhibition of cyclooxygenase-2 expression, adhesion of monocytes to human umbilical vein endothelial cells, and expression of cellular adhesion molecules. *Arch. Pharm. Res*. 30: 1318-1327.
24. Srisook, K., Srisook, E., Nachaiyo, W., Chan-In, M., Thongbai, J., Wongyoo, K., Chawsuanthong, S., Wannasri, K., Insasuwan, S. and Watchranawee, K. 2015. Bioassay-guided isolation and mechanistic action of anti-inflammatory agents from *Clerodendrum inerme* leaves. *J. Ethnopharmacol*. 165: 94-102.