

Contents lists available at ScienceDirect

Asian Pacific Journal of Tropical Biomedicine

journal homepage:www.elsevier.com/locate/apjtb



Document heading doi:10.1016/S2221-1691(12)60288-3 ©2012 by the Asian Pacific Journal of Tropical Biomedicine. All rights reserved.

Phytochemical characterization and antimicrobial activity of *Curcuma xanthorrhiza* Roxb.

Mary Helen PA¹, Susheela Gomathy K², Jayasree S¹, Nizzy AM¹, Rajagopal B¹, Jeeva S^{3*}

¹Department of Biotechnology, Malankara Catholic College, Tamil Nadu, India ²Department of Bioinformatics, National College of Arts and Science, Kerala, India ³Department of Botany, Scott Christian College, Tamil Nadu, India

ARTICLE INFO

Article history: Received May 2012 Received in revised form 6 May 2012 Accepted 9 August 2012 Available online 28 August 2012

Keywords: Antimicrobial activity GC/MS Phytochemistry Curcuma xanthorrhiza

ABSTRACT

Objective: To study the antimicrobial activity and phytochemical characterization of essential oil isolated from the rhizome of *Curcuma xanthorrhiza* against pathogenic bacteria and fungi. **Methods:** Fresh rhizomes of *Curcuma xanthorrhiza* were subjected to hydro distillation process to obtain essential oil and characterized by Gas Chromatography– Mass Spectroscopy (GC–MS). The essential oil was evaluated for antibacterial and antifungal activity against thirteen pathogenic bacteria and six fungi by the disc diffusion method. **Results:** GC – MS analysis of the essential oil extracted from the rhizome of *Curcuma xanthorrhiza* contained the derivatives of xanthorihizol, camphene and curcumene, monoterpene hydrocarbons, oxygenated monoterpenes, sesquiterpene, hydrocarbons and other minor compounds. The antimicrobial activity of the oil showed significant inhibitory activity against the human pathogenic bacteria, no activity was observed against the fungi *Aspergillus niger* and *Fusarium oxysporum*. **Conclusions:** The findings of the present study indicate that the rhizome extract of *Curcuma xanthorrhiza* possess secondary metabolites and potential to develop antimicrobial drugs.

1. Introduction

The frequency of life-threatening infections caused by pathogenic microorganisms has increased worldwide, becoming an important cause of morbidity and mortality in immuno compromised patients in developing countries [1]. Although a large number of antimicrobial agents have been discovered, pathogenic microorganisms are constantly developing resistance to these agents ^[2]. Antibiotics are sometimes associated with side effects whereas there are some advantages of using antimicrobial compounds of medicinal plants. The later has fewer side effects, better patient tolerance, relatively less expensive, acceptance due to long history of use and being renewable in nature ^[3].

Antibacterial constituents of medicinal plants and their use for the treatment of microbial infections as possible alternatives to synthetic drugs to which many infectious microorganisms have become resistant seem to be very much promising [4]. Over the past 20 years, there has been

Tel: +91 9952202112 E-mail: solomonjeeva@gmail.com a lot of interest in the investigation of natural materials as sources of new antibacterial agents. Different extracts from medicinal plants were tested and some natural products were approved as new antibacterial drugs ^[5]. The medicinal value of plants lies in some chemical substances that produce a definite physiological action on the human body ^[6–10]. The most important of these biologically active constituents of plants are alkaloids, flavonoids, tannins and phenolic compounds ^[11–15].

In the last few years, a number of studies have been conducted in different countries to prove the antimicrobial efficacy of the bioactive compounds [16–21]. However, there is still an urgent need to identify novel substances active against pathogens with higher resistance. In view of this fact the present study was aimed to evaluate the phytochemical constituents and antibacterial activity of the rhizome extracts of *Curcuma xanthorrhiza*, commonly known as false turmeric.

2. Materials and methods

Rhizomes of *Curcuma xanthorrhiza* was collected from the tropical forests of Bonaccord in the Agastyamala Hills

 $^{* \}rm Corresponding$ author: Dr. S. Jeeva, Assistant Professor, Department of Botany, Scott Christian College, Nagercoil – 629 003, Kanyakumari District, Tamil Nadu, India.

of Kerala, India. The fresh rhizomes were shade dried and powdered in a mechanical blender. The powdered rhizome was subjected to hydro-distillation using a modified Clevenger-type glass apparatus for 6 hours for isolation of oils separately. The oil samples were stored at 0°C in airtight containers after drying them over anhydrous sodium sulfate and filtered before going to GC-MS analysis.

GC-MS analysis was carried out on a GC clarus 500 Perkin Elmer system comprising a AOC-20i autosampler and gas chromatograph interfaced to a mass spectrometer (GC-MS) instrument employing the following conditions: column Elite-1 fused silica capillary column (30×0.25 mm ID ×1EM df, composed of 100% Dimethyl poly siloxane), operating in electron impact mode at 70 eV; helium (99.999%) was used as carrier gas at a constant flow of 1ml/min and an injection volume of 0.5 EI was employed (split ratio of 10:1) injector temperature 250°C; ion-source temperature 280°C. The oven temperature was programmed from 110°C (isothermal for 2 min), with an increase of 10°C/min, to 200°C/min, then 5°C/ min to 280°C/min, ending with a 9 min isothermal at 280°C. Mass spectra were taken at 70 eV; a scan interval of 0.5 s and fragments from 40 to 550 Da.

Interpretation on mass spectrum of GC-MS was done using the database of National Institute Standard and Technology (NIST) having more than 62,000 patterns. The mass spectrum of the unknown component was compared with the spectrum of the known components stored in the NIST library. The name, molecular weight and structure of the components of the test materials were ascertained.

Antimicrobial study was carried out by disc diffusion method (Bauer et al., 1966) against the pathogens viz. Bacillus megaterium (MTCC 428), Proteus vulgaris (MTCC 1771), Bacillus amyloliquefaciens (MTCC 2248), Streptococcus thermophilus (MTCC 1938), Xanthomonas compestris (MTCC 2289), Shigelli sonnei (MTCC 2957), Enterobacter aerogens (MTCC 2990), E.coli1 (MTCC1), Mycobacterium sp. (MTCC 290), Salmonella typhi (MTCC 734), Klebsiella pneumoniae (MTCC 3040), Staphylococcus aureus (MTCC 3103), Pseudomonas aeruginosa (MTCC 2642). The fungal strains are Aspergillus niger (MTCC 281), Aspergillus flavus (MTCC 2456), Candida albicans (MTCC 3018), Penicillium chrysogenum (MTCC 947), Fusarium oxysporum (MTCC 2480) and Kluveromyces maxianus (MTCC 1389). The microbial strains were procured from Microbial Type Culture Collection (MTCC), Institute of Microbial Technology, Sector 39-A, Chandigarh, U.T., 160-036, India.

3. Results

The GC–MS analysis of the essential oil extracted from the rhizome of *Curcuma xanthorrhiza* showed Xanthorrhizol (64.38%) is the major compound followed by Camphene (8.27%), Curcumin (5.85%), $_{\alpha}$ Pinene (1.93%), $_{\alpha}$ thujene (0.16%), $_{\beta}$ – Pinene (0.14%), Myrcene (0.37%), Linalool (0.27%) and Zingiberene (0.10%) on comparison with the mass spectra of the constituents with the NIST library.

The antimicrobial activity of essential oil extract from *Curcuma xanthorrhiza* rhizome was tested against thirteen pathogenic bacteria and six fungi. In terms of antibacterial activity, the essential oil showed remarkable antibacterial activity with zone of inhibition of 14mm each against E. coli and Bacillus amyloliquefaciens, followed by

Klebsiella pneumoniae (12mm), Shigella sonnei (11mm) and Enterobacter aerogens (10mm). Three bacteria Pseudomonas aeruginosa, Salmonella typhi and Xanthomonas campestris displayed the inhibition zone of 9mm each and Mycobacterium sp., Proteus vulgaris, Streptococcus thermophilus and Staphylococcus aureus showed each 8mm of inhibitory activity, whereas Bacillus megaterium showed 7mm activity against the essential oil isolated from the rhizome of *Curcuma xanthorrhiza*.

In order to find out the antifungal activity of chemicals present in the rhizome of *Curcuma xanthorrhiza* six species of fungus were tested. Of these, Candida albicans and Kluyveromyces maxianus exposed the maximum and minimum inhibitory zones of 9mm and 7mm respectively. Aspergillus flavus and Penicillium chrysogenum showed the inhibitory zone of 8mm each. However it is evident that, *Aspergillus niger* and *Fusarium oxysporum* were resistant to the essential oil extract. The overall inhibitory effect of *Curcuma xanthorrhiza* extract revealed the better activity against the pathogenic bacteria than fungus.

4. Discussion

Medicinal plants have been used for centuries as remedies for human diseases, because they contain components of therapeutic value [22-26]. Extraction of bioactive compounds from medicinal plants permits the demonstration of their physiological activity. It also facilitates pharmacology study leading to the synthesis of more potent drugs for meeting demand for effective and safe use. In the present study, the plant collected from Western Ghats was identified according to their taxonomical characters as Curcuma xanthorrhiza belongs to the family Zingiberaceae. There are several data in the literature indicating a great variety of pharmacological activities of oil extracted from the members of the family Zingiberaceae, which exhibit antiallergic [27], antimicrobial [28-33], anti-inflammatory [34], antihyperlipidaemic [35] anti-nociceptive, anti-psychiatric [36], antioxidant [37, 38], hepatoprotective and immunomodulatory [39] and cytotoxic [40] activities.

The antimicrobial activity of oil extracted from *Curcuma xanthorrhiza* could be attributed to the broad spectrum of bioactive chemical compounds. On hydrodistillation of fresh rhizomes, about 0.44% of white coloured, pleasant smelling oil was obtained from *Curcuma xanthorrhiza*. Based on GC/MS analysis the major compound was identified a sesquiterpenoid compound, xanthorhizol. It is evident that Xanthorrhizol isolated from the methanol extract Curcuma xathorrhiza showed potent antibacterial [41] and anticandidal activity [42].

Curcumin (diferuoyl methane), a yellow pigment is a phenolic compound and a major phytochemical constituent of Curcuma species, has been linked with suppression of inflammation; angiogenesis; tumorigenesis; diabetes; diseases of the cardiovascular, pulmonary, and neurological systems, of skin, and of liver; loss of bone and muscle; depression; chronic fatigue; and neuropathic pain ^[43]. Recent literature revealed that curcumin has antioxidant and radical scavenging activity ^[44]. The bioconjugates having curcumin covalently attached to piperic acid, glycine, glycyl-piperic acid, alanine and acetic acid through its free phenolic groups show better antibacterial and antifungal activities via-à-vis curcumin against some common pathogenic microbes viz. Escherichia coli, Pseudomonas aeruginosa, Pseudomonas pyocynin, Candida krusei GO3 and Candida albicans (yeast). These activities have been found to be equivalent to that of the marketed drugs, Cefepime (antibacterial) and flucanozole (antifungal) ^[45].

It has been found that curcumin inhibits Bacillus subtilis and Escherichia coli growth by inhibiting FtsZ assembly ^[46]. It has also shown a wide–spectrum of chemopreventive, antioxidant and antitumor properties. Although its promising chemotherapeutic activity, preclinical and clinical studies highlight curcumin limited therapeutic application due to its instability in physiological conditions ^[47]. A synthesized curcumin analog, 1,5–diaryl–3–oxo–1,4–pentadiene such as GO–Y030, has the improved anti–tumor potential in vitro as well as in mouse model of colorectal carcinogenesis ^[48].

The mutagenicity studies showed that curcumin, as well as Curcumin- β -diglucoside, afforded high protection against the mutagenicity of sodium azide to Salmonella typhimurium TA 1531 and TA 98. Also, Curcumin-βdiglucoside exhibited higher antibacterial properties against Staphylococcus aureus and Escherichia coli but showed lower activity against Bacillus cereus and Yersinia enterocolitica than did curcumin. The results clearly demonstrate that conjugation of the phenolic hydroxyl group of curcumin to a sugar moiety rendered it water-soluble whilst retaining/enhancing its in vitro antioxidant, antimutagenic and antibacterial properties [49]. Curcuminoids and other natural and synthetic curcuminoids possess various bioactivities including anti-inflammatory, anti-oxidant, anti-HIV, chemopreventive and anti-prostate cancer effects. Recent studies on curcuminoids, particularly on curcumin, have discovered not only much on the therapeutic activities, but also on mechanisms of molecular biological action and major genomic effects [50].

Overall, the present study, along with the previous studies, shows that diverse phytochemical components present in the various species of Curcuma, including the presently studied *Curcuma xanthorrhiza* are having potent antimicrobial activity. The particular bioactive compounds responsible for antimicrobial activity, whether xanthorrhizol / curcumin or other, has yet to be confirmed. **Conflict of interest statement**

We declare that we have no conflict of interest.

Acknowledgements

The authors are grateful to Rev. Fr. Prem Kumar (Correspondent and Secretary) and the Staff Members of Biotechnology Department, Malankara Catholic College, Mariagiri, Kanyakumari, Tamilnadu, India for their constant encouragement and support.

References

- Ara N, Nur MH, Amran MS, Wahid MII, Ahmed M. In vitro antimicrobial and cytotoxic activities of leaves and flower extracts from Lippia alba. *Pakistan Journal of Biological Sciences* 2009; **12**(1): 87–90.
- [2] Al-Bari MA, Sayeed MA, Rahman MS, Mossadik MA. Characterization and antimicrobial activities of a phenolic acid derivatie produced by Streptomyces bangladeshiensis a novel species collected in Bangladesh. *Res J Med Sci* 2006; 1: 77–81.
- [3] Reddy LJ, Jose B. Evaluation of antibacterial activity of the bark, flower and leaf extracts of Gliricidia sepium from south India. *International Journal of Current Pharmaceutical Research* 2010; 2(3): 18–20.
- [4] Bari MA, Islam W, Khan AR, Mandal A. Antibacterial and antifungal activity of Solanum torvum (solanaceae). *Int J Agric Biol* 2010; **12**: 386–390.
- [5] Chehregani A, Azimishad F, Alizade HH. Study on antibacterial effect of some Allium species from Hamedan–Iran. Int J Agric Biol 2007; 9(6): 873–876.
- [6] Ahsan MR, Islam KM, Haque ME, Mossaddik MA. In vitro antibacterial screening and toxicity study of some different medicinal plants. *World Journal of Agricultural Sciences* 2009; 5(5): 617-621.
- [7] Balakumar S, Rajan S, Thirunalasundari T, Jeeva S. Antifungal activity of Ocimum sanctum Linn. (Lamiaceae) on clinically isolated dermatophytic fungi. Asian Pacific Journal of Tropical Medicine 2011; 4(8): 654–657.
- [8] Rajan S, Thirunalasundari T, Jeeva S. Anti-enteric bacterial activity and phytochemical analysis of the seed kernel extract of Mangifera indica Linnaeus against Shigella dysenteriae (Shiga, corrig.) Castellani and Chalmers. *Asian Pacific Journal of Tropical Medicine* 2011; 4(4): 294–300.
- [9] Balakumar S, Rajan S, Thirunalasundari T, Jeeva S. Antifungal activity of Aegle marmelos (L.) Correa (Rutaceae) leaf extract on dermatophytes. *Asian Pacific Journal of Tropical Biomedicine* 2011; 1(4): 309–312.
- [10] Anpin Raja RD, Jeeva S, Prakash JW, Johnson M, Irudayaraj V. Antibacterial activity of selected ethnomedicinal plants from South India. Asian Pacific Journal of Tropical Medicine 2011; 4(5): 375–378.
- [11] Kala S, Johnson M, Raj I, Bosco D, Jeeva S, Janakiraman N. Preliminary phytochemical analysis of some selected medicinal plants of south India. *Journal of Natura Conscientia* 2011; 2(5): 478–481.
- [12] Kiruba S, Mahesh M, Nisha SR, Miller Paul Z, Jeeva S. Phytochemical analysis of the flower extracts of Rhododendron arboreum Sm. ssp. nilagiricum (Zenker) Tagg. Asian Pacific Journal of Tropical Biomedicine 2011; 1: S278–S280.
- [13] Mithraja MJ, Johnson M, Mahesh M, Miller Paul Z, Jeeva S. Phytochemical studies on Azolla pinnata R. Br., Marsilea minuta L. and Salvinia molesta Mitch. Asian Pacific Journal of Tropical Biomedicine 2011; 1: S26–S29.
- [14] Kiruba S, Mahesh M, Miller Paul Z, Jeeva S. Preliminary phytochemical screening of the pericarp of Crataeva magna (Lour.) DC. – a medicinal tree. Asian Pacific Journal of Tropical Biomedicine 2011; 1: S129–S130.
- [15] Jeeva S., Johnson M., Aparna JS, Irudayaraj V. Preliminary phytochemical and antibacterial studies on flowers of selected medicinal plants. *International Journal of Medicinal and Aromatic Plants* 2011.1(2): 107-114.
- [16] Sabir MS, Ahmad DS, Hussain IM, Tahir KM. Antibacterial activity of Elaeagnus umbellata (Thunb.) a medicinal plant from Pakistan. Saudi Med J 2007; 28(2): 259–263.

- [17] Sukumarn S, Kiruba S, Mahesh M, Nisha SR, Miller Paul Z, Ben CP, Jeeva S. Phytochemical constituents and antibacterial efficacy of the flowers of Peltophorum pterocarpum (DC.) Baker ex Heyne. *Asian Pacific Journal of Tropical Medicine* 2011; **4**(9): 735–738.
- [18] Suresh Kumar P. Anti-fungal activity of Leptadenia reticulata in rat animal model in vivo. *J Basic Applied Bio* 2008; **2**(1): 9–13.
- [19] Suresh SN, Nagarajan N. Preliminary phytochemical and antimicrobial activity analysis of Begonia malabarica Lam. *Journal of Basic and Applied Biology* 2009; 3(1&2): 59-61.
- [20] Rajan S, Jeevagangai TJ. Studies on the antibacterial activity of Aegle marmelos – fruit pulp and its preliminary phytochemistry. *Journal of Basic and Applied Biology* 2009; 3(1&2): 76–81.
- [21] Pugazharasi G, Meenakshi SA, Ramesh Kannan N, Bastin Churchill M, Natarajan E. Screening of antimicrobial activity of Phyllanthus maderaspatensis L. *Journal of Basic and Applied Biology* 2009; 3(3&4): 43–49.
- [22] Premkumar G, Sankaranarayanan R, Jeeva S, Rajarathinam K. Cytokinin induced shoot regeneration and flowering of Scoparia dulcis L. (Scrophulariaceae) – an ethnomedicinal herb. Asian Pacific Journal of Tropical Biomedicine 2011; 1(3): 169–172.
- [23] Jeeva S, Jasmine T Sawian, Febreena G Lyndem, Laloo RC, Venugopal N. Medicinal plants in Northeast India: past, present and future scenario. In: National Seminar on Past, Present and Future Scenario in Medicinal Plants and Phytochemistry, organized by Department of Plant Science, Bharathidasan University, Thiruchirappalli, Tamil Nadu; 2007.
- [24] Kingston C, Jeeva S, Jeeva GM, Kiruba S, Mishra BP, Kannan D. Indigenous knowledge of using medicinal plants in treating skin diseases in Kanyakumari District, Southern India. *Indian Journal* of Traditional Knowledge 2009; 8(2): 196–200.
- [25] Jeeva GM, Jeeva S, Kingston C. Traditional treatment of skin diseases in South Travancore, southern peninsular India. *Indian Journal of Traditional Knowledge* 2007; 6(3): 498–501.
- [26] Anpin Raja RD, Prakash JW, Jeeva S. Antibacterial activity of some medicinal plants used by Kani tribe, southern Western Ghats, Tamilnadu, India. In: Trivedi PC, Editor. Ethnic Tribes and Medicinal Plans, Pointer Publishers, Jaipur; 2010: 28–45.
- [27] Tewtrakul S, Subhadhirasakul S. Anti-allergic activity of some selected plants in the family Zingiberaceae family. Journal of Ethnopharmacology 2007; 109(3): 535–538.
- [28] Indrayan AK, Garg SN, Rathi AK, Sharma V. Chemical composition and antimicrobial activity of the essential oil of Alpinia officinarum rhizome. *Indian Journal of Chemistry* 2007; 46B (12): 2060–2063.
- [29] Ibrahim H, Aziz AN, Syamsir DR, Ali NAM, Mohtar M, Ali RM, Awang K. Essential oils of Alpinia conchigera Griff. and their antimicrobial activities. *Food Chemistry* 2009; **113**(2): 575–577.
- [30] Chudiwal AK, Jain DP, Somani RS. Alpinia galanga Willd. an overview on phyto-pharmacological properties. *Indian Journal of Natural Products and Resources* 2010; 1(2): 143–149.
- [31] Kader G, Nikkon F, Rashid MA, Yeasmin T. Antimicrobial activities of the rhizome extract of Zingiber zerumbet Linn. Asian Pacific Journal of Tropical Biomedicine 2011; 1(5): 409–412.
- [32] Patel RV, Thaker VT, Patel VK. Antimicrobial activity of ginger and honey on isolates of extracted carious teeth during orthodontic treatment. Asian Pacific Journal of Tropical Biomedicine 2011; 1(S1): S58–S61.
- [33] Sivasothy Y, Chong WK, Hamid A, Eldeen IM, Sulaiman SF, Awang, K. Essential oils of Zingiber officinale var. rubrum Theilade and their antibacterial activities. *Food Chemistry* 2011; 124(2): 514–517.
- [34] Dugasani S, Pichika MR, Nadarajah VD, Balijepalli MK, Tandra S, Korlakunta JN. Comparative antioxidant and anti-inflammatory effects of (6)-gingerol, (8)-gingerol, (10)-gingerol and 0-shogaol.

Journal of Ethnopharmacology 2010; 127(2): 515-520.

- [35] Ling J, Wei B, Ly G, Ji H, Li S. Anti-hyperlipidaemic and antioxidant effects of turmeric oil in hyperlipidaemic rats. *Food Chemistry* 2012; **130**(2): 229–235.
- [36] Lee J, Ah Kim K, Jeong S, Lee S, Park, HJ, Kim NJ, Lim S. Antiinflammatory, anti-nociceptive, anti-psychiatric effects by the rhizomes of Alpinia officinarum on complete Freund's adjuvantinduced arthritis in rats. *Journal of Ethnopharmacology* 2009; 126(2): 258–264.
- [37] Chan EWC, Lim YY, Wong LF, Lianto FS, Wong SK, Lim KK, Joe CE, Lim TY. Antioxidant and tyrosinase inhibition properties of leaves and rhizomes of ginger species. *Food Chemistry* 2008; 109(3): 477–483.
- [38] Wijekoon NMJO, Bhat R, Karim AA. Effect of extraction solvents on the phenolic compounds and antioxidant activities of bunga kantan (Etlingera elatior Jack.) inflorescence. *Journal of Food Composition and Analysis* 2011; 24(4–5): 615–619.
- [39] Sengupta M, Dharma GD, Chakraborty B. Hepatoprotective and immunomodulatory properties of aqueous extract of Curcuma longa in carbon tetra chloride intoxicated Swiss albino mice. Asian Pacific Journal of Tropical Biomedicine 2011; 1: 193–199.
- [40] Hossain S, Kader G, Nikkon F, Yeasmin T. Cytotoxicity of the rhizome of medicinal plants. Asian Pacific Journal of Tropical Biomedicine 2012; 2: 125–127.
- [41] Hwang JK, Shim JS, Pyun YR. Antibacterial activity of xanthorrhizol from *Curcuma xanthorrhiza* against oral pathogens. Fitoterapia 71(3): 321–323.
- [42] Rukayadi Y, Yong D, Hwang J. In vitro anticandidal activity of xanthorrhizol isolated from *Curcuma xanthorrhiza* Roxb. *Journal* of Antimicrobial Chemotherapy 2006; 57: 1231–1234.
- [43] Anand P, Thomas SG, Kunnumakkara AB, Sundaram C, Harikumar KB, Sung B et al. Biological activities of curcumin and its analogues (congeners) made by man and mother nature. *Biochemical Pharmacology* 2008; **76**(11): 1590–1611.
- [44] Ak T, Gulcin I. Antioxidant and radical scavenging properties of curcumin. *Chemico–Biological Interactions* 2008; **174**(1): 27–37.
- [45] Mishra S, Narain U, Mishra R, Misra K. Design, development and synthesis of mixed bioconjugates of piperic acid–glycine, curcumin–glycine/alanine and curcumin–glycine–piperic acid and their antibacterial and antifungal properties. *Bioorganic and Medicinal Chemistry* 2005; 13(5): 1477–1486.
- [46] Kaur S, Modi NH, Panda D, Roy N. Probing the binding site of curcumin in Escherichia coli and Bacillus subtilis FtsZ – a structural insight to unveil antibacterial activity of curcumin. *European Journal of Medicinal Chemistry* 2010; 45(9): 4209–4214.
- [47] Basile V, Ferrari E, Lazzari S, Belluti S, Pignedoli F, Imbriano C. Curcumin derivatives: molecular basis of their anti-cancer activity. *Biochemical Pharmacology* 2009; **78**(10): 1305–1315.
- [48] Kudo C, Yamakoshi H, Sato A, Nanjo H, Ohori H, Ishioka C, Iwabuchi Y, Shibata H. Synthesis of 86 species of 1,5-diaryl-3oxo-1,4-pentadienes analogs of curcumin can yield a good lead in vivo. BMC Pharmacology 2011; 11: 4. doi:10.1186/1471-2210-11-4.
- [49] Parvathy KS, Negi PS, Srinivas P. Antioxidant, antimutagenic and antibacterial activities of curcumin-β-diglucoside. Food Chemistry 2009; 115(1): 265-271.
- [50] Itokawa H, Shi Q, Akiyama T, Morris-Natschke SL, Lee K. Recent advances in the investigation of curcuminoids. *Chinese Medicine* 2008; **3**: 11. doi:10.1186/1749-8546-3-11.