Pharmacological Assessments of Hibiscus rosa-sinensis Plant: A Comprehensive Review

***Ritu Agarwal, [1]Archana Jadoun**

***Research Scholar, Shri Ramdeobaba College of Pharmacy, Jabalpur**

[1]Research Scholar, Shri Ramdeobaba College of Pharmacy, Jabalpur

Abstract: Recently, a variety of synthesized medicine side effects have prompted researchers to turn to plant species as a trustworthy resource of cutting-edge treatment. One of the biggest adversaries of contemporary medicine is pain. Pain is a worldwide community healthcare issue that has a significant negative effect on living style and a significant economic burden. According to estimates, nearly 80% of people in the globe utilize plants as analgesics or antinociceptive medications in conventional treatments. Hibiscus species are extensively used for their phytoconstituents and therapeutic approaches research. The goal of the existing research was to discuss the various pharmacological potential of *Hibiscus rosa-sinensis* plant extracts. The review has been prepared based on the literature survey on scientific journals and electronic sources.

Keywords: *Pain, analgesics, inflammation, nociceptors, Pain Theory, Hibiscus rosa-sinensis*

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Corresponding Author- rituagarwal21@gmail.com*

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Introduction

Pain is a hostile sensory and sensitive incident accompanied with authentic or prospective tissue damage or designated in relations of such. The word comes from the Latin verb "to pain", meaning "to feel pain", via Middle English pene, which shares a Proto-Germanic root with "chemical pain" [1].

Pain can be considered as the body's alert mechanism or warning signal that something might be wrong or that a threat exists. Although pain is subjective and can have

many possible causes, it is widely accepted to occur when specialized nociceptors of the peripheral nervous system are activated by a particular physical stimulus [2]. The most common ways of classifying pain are by duration, location and intensity. Pain sensation may arise from within the body (such as during inflammation), or outside of it (as in the case of tissue damage caused by trauma, heat or cold). Pain may be characterized by its intensity on a measure that runs from "no pain" to "the most pain" [3]. The stimulation of the pain receptors in the principal afferent fibres, including the myelinated As-fiber and unmyelinated C-fiber, has been interrelated to the sensitivity of pain. Both nociceptors are passive whenever there is minimal discomfort and homeostasis is preserved. Once a potentially harmful stimulus is prominent, they become activated. Therefore for brain to identify pain and generate a reaction to the menace, it needs to perceive a succession of sensory stimuli [4].

The study of pain is known as palliative science which can include both research and studies related to the treatment of pain and individual experiences of people living with persistent pain. Classified according to its duration, location, mechanism, intensity and quality, it can be acute or chronic [5]. Emergency medical services are dispatched when there is immediate risk of life-threatening harm from loss of blood plasma or excessive internal bleeding. The causes of most acute pain are relatively straightforward for experts in that field; for example, headaches may result from a brain tumor in rare cases but tend to occur following serious head injury. The feeling of pain often progresses through three major levels [6]. The peripheral nervous system sends signals to the dorsal horn (DH), which is positioned in the spinal cord, during the second stage after the first stage of pain sensitivity (PNS). The third stage culminates with the central nervous system's role in signal transmission to the higher brain (CNS) [7].

Nociceptors and the Pain Pathways

A highly specialized sensory receptors known as nociceptors are in charge of detecting noxious (painful) stimuli and converting them into electrical signals that are then transmitted to the central nervous system. These are the major afferent fibres Ad and C's unbound nerve synapses. These might potentially activated by mechanical, thermal, or chemical stimuli and are dispersed all across the system (skin, viscera, muscles, joints, meninges) [8].

Damaged tissue releases inflammatory mediators, including as bradykinin, serotonin, prostaglandins, cytokines, and H+, which might explicitly trigger nociceptors. They could also work to lower the nociceptors' stimulation thresholds so that minimal amplification has been needed to activate them. This procedure is called as Primary sensitization [9].

The two pathways are responsible to carry signals to the brain. The ascending route and the descending route. The word "ascending pathway" refers to nerves that carry sensory signals headwaters from the spinal cord to the brain, whereas the word "descending pathway" refers to nerves that supply reflex information downstream from the brain across the spinal cord. [10].

Classification of Pain

The International Association for the Study of Pain (IASP) states three major systems of pain classification:

i. The non-taxonomic system, is based on how pain is caused or experienced.

ii. The second classifies pain by its symptoms, with each type having a distinct pattern of clinical features.

iii. The third taxonomic system divides pain into two major categories: neuropathic (or neurological) and nociceptive pains [11].

Principles of Pain Contrivance

As because there is an existence of noxious stimuli, the elementary pain concept has been divided into three processes - transduction, transmission, and modulation.

Transduction- All along with nociceptive route, transduction happens in the mentioned sequence:

- Provocation incidents are transformed into chemical tissue activities;
- Chemical tissue and synaptic cleft activities are therefore transformed into electrical incidents in the neurons;
- Electrical actions in the neurons are then transduced as chemical episodes at the synapses [12].

Transmission- The subsequent step after transduction would be transmission. Transmitting electrical sensations along the brain pathways is how neurotransmitters in the synaptic cleft convey messages from a

post-synaptic terminal of one cell to a pre-synaptic terminal of another. [11].

Modulation- In the meantime, the principal afferent neuron, DH, and elevated brain centers being adopted to up- or down-regulate the modulation event at all levels of nociceptive routes. Each of such, ultimately culminate to a certain phenomenon: the route of pain has indeed been started and finished, letting individuals to experience the unpleasant sensations that the provocation has caused [13].

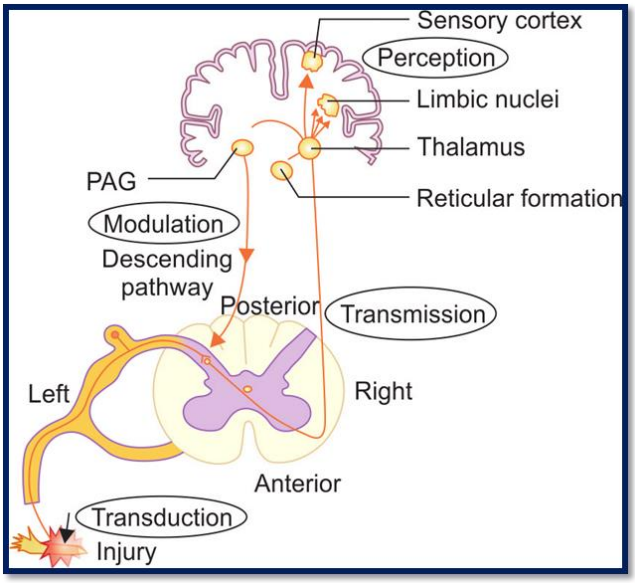

Fig.1 Basic Pain Mechanism [12, 13]

Gate Control Theory of Pain

The opening in the spinal cord make a distinction between fiber sorts while conveying pain impulses, as contradict to a real gateway that open up and shuts to permit all entities to travel across. In particular, since vibrations from massive nerve strands are suppressed, pain sensations produced by small nerve fibres may transmit. Scientists Ronald Melzack and Patrick Wall presented the gate control hypothesis of pain in a study that was presented in 1965. The objective was to shed light on how psychological circumstances could make anything feel more uncomfortable by rendering it even harsher or by developing it tougher [12]. This procedure, according to Melzack and Wall, could account for our propensity to rub wounds after they occur. Increased regular tactile sensory signals helps to reduce pain sensation by decreasing the functioning of pain fibres.

Gate control theory posits that pain is not always simply the result of nociceptive input. Instead, it is a complex phenomenon that involves both peripheral and central nervous system processes. The gate control concept suggests that there are various levels at which pain can be modulated, and that different interventions may work better or worse depending on the individual's particular situation. This theory has led to a greater understanding of pain and its treatment, and has helped to develop more effective pain management strategies. [14].

Gate control theory of pain proposes that pain is the result of a gate control mechanism in the nervous system. The gate is opened by stimuli that activate nociceptive receptors (pain-sensing neurons), and closed by other input, such as from non-nociceptive receptors or the brain itself. This theory suggests that pain perception can be modulated by changing the balance of activity between these different types of inputs [13, 14].

Pharmacological activities of *Hibiscus rosa-sinensis* as a pain reliever

K Hema et al., (2022) investigated *Hibiscus rosa-sinensis* Linn's young blossom ethyl acetate fraction for its anti-inflammatory properties. Crimson blood cell stability brought on by in vitro hypotonicity has been used to analyse double yellow flowers with red centers. Erythrocytes subjected with a hypotonic liquid were investigated for their response to an inflammatory situation. It has been discovered that the ethyl acetate fraction exhibited cell wall stabilizing ability, peaking at 100 g. *Hibiscus rosa-sinensis* Linn. ripe blooms weighing 3000 g had been selected, harvested, and processed for 3 days using 90% methanol with boiling. The alcoholic extract subsequently strained under vacuum, and the aqueous solution has been segregated with roughly by using benzene (2L), peroxide-free diethyl ether, and ethyl acetate as the carriers. Since flavonoids are polyphenolic chemicals and have anti-inflammatory properties, it has been demonstrated that they have a significant anti-inflammatory influence especially at a comparatively modest quantity of 100 g of ethyl acetate component. As an outcome, it was found that the ethyl acetate extract derived from *Hibiscus rosa-sinensis* Linn. Seemed very effective towards all or particular aspect of severe or persistent aggravation. [15].

B. Mounika (2019) formulated and evaluated the anti-inflammatory emulgel by using methanolic extract of hibiscus rosa sinensis. Different oils had been utilised for

the development of emulsions. The best-optimized emulsion was converted into an emulgel using several gelling agents in various ratios, based on its physicochemical properties. Based on their physical-chemical characteristics and percentage of drug release, the generated emulgel formulations were finally optimised. A model of rat paw oedema caused by carrageenan was used to test the anti-inflammatory efficacy of the improved formulation [16].

K.G. Singh et al., (2018) studied the tea extracts from different plant species (Camellia sinensis, Hibiscus rosa sinensis, Rosa, Zingiber officinale, and Matricaria chamomilla), for anti-oxidant, anti-inflammatory, and anti-arthritic characteristics. Ex-vivo studies were conducted using liver tissue to assess the antioxidant properties of the samples. To further evaluate the sample's anti-inflammatory effects, experiments like preventing protein denaturation and stabilizing RBC membranes were carried out. Chicken collagen was used in the collagen denaturation assay to test the materials' anti-arthritic abilities. The specimens passed every test, indicating that they were effective in their anti-oxidant, anti-inflammatory, and anti-arthritic actions. Because there are no side effects, using organic substances to combat illnesses has therefore emerged as a more viable choice [17].

Zubia Begum (2018) proposed *Hibiscus rosa-sinensis* is a perennial flowering shrub native to East Asia. The root of the plant has been used traditionally in Chinese and Ayurvedic medicine for the treatment of various ailments such as indigestion, fever, and inflammation. Modern scientific research has shown that *Hibiscus rosa-sinensis* root extract has analgesic and anti-inflammatory properties in animal models of disease. In this study, they investigated the efficacy of *Hibiscus rosa-sinensis* root extract in reducing pain and inflammation in albino rats. We found that *Hibiscus rosa-sinensis* root extract significantly reduces both pain and inflammation in rats without causing any adverse side effects. These results suggest that *Hibiscus rosa-sinensis* root extract may be a safe and effective natural remedy for the treatment of pain and inflammation [18].

Zubia et al., (2015) emphasises the phytochemical contents, anti-inflammatory, analgesic, and antipyretic properties of *Hibiscus rosa-sinensis*. The methanolic extract of the whole plant showed significant anti-inflammatory activity in carrageenan-

induced paw edema in rats at a dose of 200 mg/kg. The aqueous extract of Hibiscus rosa-sinensis was found to possess analgesic activity in mice based on the tail immersion and acetic acid–induced writhing methods. The ethanolic extract of Hibiscus rosa-sinensis demonstrated good antipyretic activity in yeast-induced pyrexia in rats and rabbits, which may be due to its central nervous system depressant effect [19].

Siti Zahela et al., (2013) examined and contrasted the anti-inflammatory properties of ethanol extracts of the flower and leaf from two different species of plant, i.e., *Hibiscus rosa-sinensis* L. and var alba. Carrageenan with 0.1ml, has been given sub-plantar 30 minutes prior to the dosing of the extracts (5, 50, or 100 mg/kg) in the anti-inflammatory test. After administering carrageenan for 6 hours, the rats were put to death, and the polymorph nuclear infiltration (PNL) in the paw tissues has been quantified. Testing for phytochemicals had also been carried out. Considering the Constant Dosage Technique and controlled dosages levels, the acute dose reaction has been assessed. The findings showed that all extracts included flavonoids, saponins, and steroids. Animals dosed with all extracts up to 500 mg/kg did not experience any toxicity. Histologically, there are no abnormalities in the organs and no substantial alterations ($p>0.05$) in liver enzyme markers. *Hibiscus rosa-sinensis* L. (red specie) flower and leaves extract dosages of 50 and 100 mg/kg significantly reduced swelling ($p<0.05$). *Hibiscus rosa-sinensis* var. Alba's (white specie) flower and leaf effectively reduced swelling in all tested dose ranges (p 0.05). White hibiscus has been more powerful than red hibiscus in causing a substantial reduction (p0.05) in PNL penetration across all extract concentrations. All extracts significantly shortened the length of the licking reaction (p 0.05) [20]

Other Pharmacological activities

Pillai et al., (2016) Ethyl acetate from *Hibiscus rosa-sinensis* petals (EHRS) was tested in investigational diabetes at a dose of 25 mg/kg bw and contrasted to metformin for its ability to reduce blood sugar levels. By administering (EHRS), the increased concentrations of serum glucose (398.56 35.78) and glycated haemoglobin (12.89 1.89) in diabetic rats were dramatically reduced (156.89 14.45 and 6.12 0.49, respectively). By controlling the actions of glycogen metabolising enzymes, the blood contents of hepatotoxicity biomarker enzymes substantially controlled, and the

glycogen concentration was recovered. The activation of marker genes implicated in the signalling pathway for glucose homeostasis was markedly altered. The biochemical result was verified by a histopathological examination of the liver and pancreas [21].

Brito et al., (2015) determined the H. rosa flower and leaf decoction's preclinical anti-inflammatory, analgesic, and antipyretic effects. Application of 10 g/L of croton oil, 75 g/per ear, was used to assess activity using an acute inflammatory model (ear edoema test). 10% of the decoctions had been administered on both sides of the affected ears, and various quantities of 30% decoctions of flowers and leaves were tested topically and orally. The writhing test and the tail flick test, both conducted in water heated to 55°C, served as the analgesic model. Male OF-1 mice were used for all research studies (20–25 g). In order to investigate the antipyretic activity, male Wistar rats were given brewer's yeast (15% in water; 1 mL/100 g, sc) to induce pyrexia (180-200g). When administered topically, the leaves and floral extracts (30%) reduced inflammation in 54.7% and 30.9% of people, significantly. In contrast to the reference sample, oral doses of both extracts did not considerably reduce inflammation, but they did remarkably reduce nociception in exposure to thermal stimulation.

In each case, *H. rosa-sinensis* decoctions greatly reduced the frequency of abdominal stretches. From the first hour to four hours after administration, only the decoction of flowers demonstrated a strong antipyretic efficacy comparable to that of paracetamol [22].

Tiwari et al., (2015) determined the presence of secondary metabolites in the methanolic extracts of *H. rosa-sinensis* leaves and flowers and assessed the extract's antibacterial activity. Various doses of methanolic leaves and flowers extracts varying from 31.25 to 500 mg/disc have been studied with the positive reference gentamicin to determine how well they inhibited the growth of the bacteria E. coli and S. aureus. With an increase in extract concentration, both extracts demonstrated progressively more antibacterial activity. At a dosage of 500 mg, the optimum zones of inhibitory effect for E. coli reached 23+1.01 mm and 13.75+0.99 mm for methanolic extracts of *H. rosa-sinensis* leaves and flowers, accordingly. The highest region of inhibitory effect for S. aureus, therefore, was 19.33 + 0.29 mm and 9.75 + 0.76 mm for methanolic H. rosa sinesis leaves and

flowers extracts at concentrations of 500 mg. Such findings imply that a variety of pharmacologically potent chemicals with the propensity to serve as antibacterial agents were present in methanolic extracts of *H. rosa-sinensis* leaves and flowers, which may help alleviate infections brought on by those microbes [23].

Kandare et al., (2012) revealed the beneficial effects of a hydro alcoholic extract of *Hibiscus rosa-sinensis* foliage (HRS) in investigational colitis brought on by acetic acid in male wistar rats. A 2 mL intra rectal dose of acetic acid (4%) was given to the animals. Six rats were used and each of them received a different type of medication. As a normal medication, prednisolone was employed, and HRS was given orally at doses of 50, 100, and 200 mg/kg. Rats in the reference category were given 1 mL of liquid (distilled water). After the 11-day medication routine, variations in the ulcer region, ulcer ratio, spleen strength, and colon mass to length coefficient, macroscopic rating, hematological variables and histological variations have been noted. As a result, in acetic acid-induced colitis, exposure with HRS for 7 days had a substantial impact on reducing oxidative pressure, colonic NO, TNF-, and elevating SOD and GSH at doses of 100 and 200 mg/kg [24].

Reena J Patel et al., (2012) explained the antibacterial efficacy towards pathogenic microorganisms of 5 distinct *Hibiscus rosa-sinensis* varieties has been investigated. *Hibiscus rosa-sinensis* was investigated for its antimicrobial properties using four varied extracts against both Gram positive and Gram negative bacteria. Agar diffusion was used to test for antibacterial properties. Substantial bactericidal efficacy against the "OR-ANGE" species were demonstrated using ethyl acetate leaf extract. Ethyl acetate and methanol extracts from these four plant samples exhibited more antibacterial efficacy than the remaining extracts, but the hexane extract had very little antimicrobial effect. The examined microorganisms were subjected to ethyl acetate extract screening at the minimum inhibitory concentration (MIC). At concentration 0.625 mg ml-1, it began to exhibit inhibitory activity. The most effective solvent for extraction and antimicrobial activity was found to be methanolic extract, which was one of four distinct extracts [25].

Conclusion

Rosa sinensis is a potent medicinal plant, and research has shown that it possesses a

number of beneficial traits. Future study on the hibiscus plant has a lot of potential, notably in the areas of pharmacology and cosmeceuticals. *Hibiscus rosa-sinensis* is a medicinal plant with a wide range of pharmacological and therapeutic activities. Its flowers, leaves, and roots are all known to have medicinal effects such as oral contraception, laxative, aphrodisiac, menorrhagic, and more. Therefore, the majority of the work might be done on the aforementioned factory to uncover the unsolved mysteries that would aid the current pharmaceutical industry. *Hibiscus rosa-sinensis* is a potentially perennial herb with a broad variety of potential uses, and the systematic study evaluated its chemical components, pharmacological properties, and therapeutic value.

REFRENCES

1. Rashmi B.R, Ebrahim N.K.C, A review on pain and its signals modulation by body, IP International Journal of Comprehensive and Advanced Pharmacology, July-September, 2019;4(3):84-90

2. Aitkenhead AR, Rowbotham DJ, Smith G, eds (2001) Textbook of anaesthesia. Fourth edition. Churchill Livingstone, Edinburgh.

3. Yam, M. F., Loh, Y. C., Tan, C. S., Khadijah Adam, S., Abdul Manan, N., & Basir, R. (2018). General Pathways of Pain Sensation and the Major Neurotransmitters Involved in Pain Regulation. International journal of molecular sciences, 19(8), Pgno. 2164.

4. MacIntyre PE, Schug SA, Scott DA, Visser EJ, Walker SM; APM:SE Working
   Group of the Australian and New Zealand College of Anaesthetists and Faculty of Pain Medicine (2010), Acute Pain Management: Scientific Evidence. Third Edition. ANZCA & FPM, Melbourne

5. Serpell M. (2006) Anatomy, physiology and pharmacology of pain. Surgery 24 (10): 350-353

6. Stannard C, Booth S, eds (2004) Churchill's Pocket Book of Pain. Second edition. Churchill Livingstone, Edinburgh

7. Yam MF, Loh YC, Tan CS, Khadijah Adam S, Abdul Manan N, Basir R. General Pathways of Pain Sensation and the Major Neurotransmitters Involved in Pain

Regulation. Int J Mol Sci. 2018; Vol.19(8): Pgno.2164

8. Dubin AE, Patapoutian A. Nociceptors: the sensors of the pain pathway. J Clin Invest. 2010; Vol. 120 (11): Pgno.3760-72.

9. International Association for the Study of Pain. IASP Terminology

10. Basbaum A.I., Bautista D.M., Scherrer G., Julius D. Cellular and molecular mechanisms of pain. Cell. 2009;139:267–284.

11. Raja SN, Carr DB, Cohen M, Finnerup NB, Flor H, Gibson S, Keefe FJ, Mogil JS, Ringkamp M, Sluka KA, Song XJ, Stevens B, Sullivan MD, Tutelman PR, Ushida T, Vader K. The revised International Association for the Study of Pain definition of pain: concepts, challenges, and compromises. Pain. 2020; Vol, 161 (9): Pgno.1976-1982.

12. Hall J.E. Guyton and Hall Textbook of Medical Physiology e-Book. Elsevier Health Sciences; Philadelphia, PA, USA: 2010

13. Melzack R. Gate control theory: On the evolution of pain concepts. *Pain Forum*. 1996;5(2):128-138

14. Mendell LM. Constructing and deconstructing the gate theory of pain. Pain. 2014; Vol. 155(2): Pgno. 210-216.

15. Hema K, Rani S. V. G, Kumar G. P. In-Vitro Anti-Inflammatory Studies of Flavonoids from Hibiscus rosa-sinensis Linn. Orient J Chem 2022; 38(1), P. 36-41

16. B. Mounika I. Bala Tripura Sundari, Development and Evaluation of Anti-Inflammatory Activity of Hibiscus Emulgel, International Journal of Ayurvedic and Herbal Medicine 9:2 (2019) 3464–3476

17. K. G. Singh , S. Sonia and N. Konsoor, In-Vitro And Ex-Vivo Studies on The Antioxidant, Anti-Inflammatory And Antiarthritic Properties of Camellia Sinensis, Hibiscus Rosa Sinensis, Matricaria Chamomilla, Rosa Sp., Zingiber Officinale Tea Extracts, International Journal of Pharmaceutical Sciences And Research, 2018; 9(8). P.3543-51

18. Begum Z, Younus I, Khan H. Analgesic and anti-inflammatory activities of the ethanol extract of Hibiscus rosa sinensis Linn (roots). Pak J Pharm Sci. 2018; P- 1927-19331

19. Begum Z, Younus I, Khan H. Anti-Inflammatory, Analgesic And Anti-Pyretic Activities of Hibiscus Rosa Sinensis Linn and Phytochemicals Pak J Pharm Sci. 2015; P- 1927-19331

20. Siti Zaleha Raduan, Muhammad Wahizul Haswan Abdul Aziz, Roslida Abd Hamid, Zainul Amiruddin Zakaria, Anti-inflammatory effects of *Hibiscus rosa-sinensis* L. and *Hibiscus rosa-sinensis* var. alba ethanol extracts, International Journal of Pharmacy and Pharmaceutical Sciences 2013; 5(4): P. 754-762

21. Pillai SS, Mini S. Hibiscus rosa-sinensis Linn. petals modulates gl ycogen metabolism and glucose homeostasis signalling pathway in streptozotocin-induced experimental diabetes. Pla nt Foods Hum Nutr. 2016;71(1):42-48.

22. Brito G, Martínez I, Morón F, Victoria MC, Duménigo A, Morejón Z, Nossin E, Preclinical validation of traditional use of *Hibiscus rosa-sinensis* (marpacífico). 2015; P. 21-25

23. Udita Tiwari, Poonam Yadav, and Darshika Nigam, Study on Phytochemical Screening and Antibacterial Potential of Methanolic Flower and Leaf Extracts of Hibiscus rosa sinensis, International Journal of Innovative and Applied Research, 2015; Volume 3, Issue (6): P. 9- 14

24. Kandhare, A. D., Raygude, K. S., Ghosh, P., Ghule, A. E., Gosavi, T. P., Badole, S. L., & Bodhankar, S. L. (2012). Effect of hydroalcoholic extract of Hibiscus rosa sinensis Linn. leaves in experimental colitis in rats. Asian Pacific Journal of Tropical Biomedicine, 2(5), 337–344.

25. Reena J Patel, Aditi Patel, Dharmesh Vaghasiya, Anju Nagee, Antimicrobial Evaluation of *Hibiscus rosa-sinensis* plant extracts against Some Pathogenic Bacteria, Bulletin of Environmental and

Scientific, 2012; Vol.1, Issue (3-4), P.14-17