Determination of Analgesic Activity of the Leaves of *Stereospermum chelonoides* DC

A Dissertation Submitted To the Department Of Pharmacy,

East West University

In The Partial Fulfillment of the Requirements for the Degree of Bachelor of Pharmacy

Submitted by

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Declaration by the Research Candidate

I, **Suraya Yasmine**, ID: 2013-1-70-060; hereby declare that the dissertation entitled, "**Determination of Analgesic Activity of the Leaves of *Stereospermum chelonoides* DC"** submitted by me to the Department of Pharmacy, East West University, in partial fulfillment of the requirements for the award of the degree of Bachelor of Pharmacy (B.Pharm) is a complete record of original research work carried out by me during 2016 under the supervision and guidance of **Meena Afroze Shanta,** Senior Lecturer, Department of Pharmacy, East West University and it has not formed the basis for the award of any other Degree/Diploma/Fellowship or other similar title to any candidate of any University.

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This is to certify that the thesis entitled **"Determination of Analgesic Activity of the Leaves of *Stereospermum chelonoides* DC"** submitted to the Department of Pharmacy, East West University, in partial fulfillment of the requirements for the award of the degree of Bachelor of Pharmacy, is a complete record of original research work carried out by **Suraya Yasmine (ID: 2013-1-70-060)** during 2016 of her research in the Department of Pharmacy at East West University, under my supervision and guidance and the thesis has not formed the basis for the award of any other Degree/Diploma/Fellowship or other similar title to any candidate of any University.

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This is to certify that the thesis entitled **'Determination of Analgesic Activity of the Leaves of *Stereospermum chelonoides* DC' submitted** to the Department of Pharmacy, East West University for the partial fulfillment of the requirement for the award of the degree Bachelor of Pharmacy, was carried out by **Suraya Yasmine (ID: 2013-1-70-060)**, during the period 2016 of her research in the Department of Pharmacy, East West University.

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Abstract

Stereospermum chelonoides (Family: Bignoniaceae), locally known as 'Dhamara', is a medicinal herb, which is traditionally been used in various ailments like infections, rheumatism and inflammation, and also cancer. But till to date, very few investigations have been made for the scientific and methodical validation of these traditional claims. Therefore, the present study was designed to investigate analgesic property of methanol and petroleum ether fractions of the leaves of *Stereospermum chelonoides* DC. Analgesic potential of methanol and petroleum ether fractions of the leaves of *Stereospermum chelonoides* was evaluated for peripheral pharmacological actions using acetic acid-induced writhing. Both the fraction, at the doses of 250 mg/kg and 500 mg/kg, displayed significant analgesic action acid in a dose dependent manner in the tested models by inhibiting pain induced by acetic and the result was statistically significant. Indomethacin was used as the standard drug in this research. From the result it was found that, the methanol extract gives inhibition 8.36 % and 51.51 % at doses of 250 mg/kg and 500 mg/kg respectively and extract of petroleum ether gives 10.03% and 31.44% inhibition at the doses of 250 mg/kg and 500 mg/kg respectively. The standard group gives 86.96% of inhibition ($p<0.001$).

Key Words: *Stereospermum chelonoides,* Acetic acid, Writhing test, Analgesic activity, Flavonoids, Narcotic and NSAIDs

Dedicated To MY Beloved

Parents

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Introduction

1.1 Introduction:

Nature dependably remains as a brilliant stamp to represent the exceptional marvel of advantageous interaction. The biotic and abiotic components of nature are all associated. The plants are fundamental to man for his life. The three essential necessities of life – sustenance, garments and protect and a large group of other helpful items are provided to us by the plant kingdom. Nature has given a total storage facility of solutions for cure all infirmities of humanity. The information of medications has amassed over a great many years as a consequence of man's curious nature so that today we have numerous viable method for guaranteeing social insurance (Daniel *et a*l., 2001).

Many higher plants produce economically important organic compounds such as oils, resins, tannins, natural rubber, gums, waxes, dyes, flavors and fragrances, pharmaceuticals, and pesticides. However, most species of higher plants have never been described, much less surveyed for chemical or biologically active constituents, and new sources of commercially valuable materials remain to be discovered. Advances in biotechnology, particularly methods for culturing plant cells and tissues, should provide new means for the commercial processing of even rare plants and the chemicals they produce. These new technologies will extend and enhance the usefulness of plants as renewable resources of valuable chemicals. (Ghani, A., 1998 and Khan, M. et al., 2001). In the future, biologically active plant-derived chemicals can be expected to play an increasingly significant role in the commercial development of new products for regulating plant growth and for insect and weed control. Recently, dramatic changes have taken place in the primary health care system of world population through the development of science, technology and medical science, but till to day 400 cores of people of the world are totally dependent on herbal medicine. It is revealed that even in the developed countries 25%, of the prescribed drugs come from plant sources and herbal medicines are used by about 7580% of the world's population for primary health care because of their better cultural acceptability, better compatibility with human body and lesser side effects (Balandrin *et al.,*2016).

1.2 Medicinal Plants

WHO defines medicinal plants in the following way:

"A medicinal plant is any plant which in one or more of its organs, contains substances that can be used for therapeutic purposes or which is a precursor for synthesis of useful drugs"

The plants that have restorative properties or apply gainful pharmacological impacts on the creature body are for the most part assigned as "Therapeutic Plants". In spite of the fact that there are no obvious morphological attributes in the therapeutic plants developing with them, yet they have some uncommon qualities that make them therapeutically imperative. It has now been built up that the plants which are naturally synthesized and contain some auxiliary metabolites, similar to alkaloids, glycosides, tannins, unstable oils and contain minerals and vitamins, have medicinal properties (Srivastava J.J. *et al.,* 1996).

1.3 Herbal medicines

Herbal medicines include herbs, herbal materials, herbal preparations and finished herbal products, that contain as active ingredients parts of plants, or other plant materials, or combinations.

1.3.1 Herbs

Crude plant material such as leaves, flowers, fruit, seed, stems, wood, bark, roots, rhizomes or other plant parts, which may be entire, fragmented or powdered.

1.3.2 Herbal materials

In addition to herbs, fresh juices, gums, fixed oils, essential oils, resins and dry powders of herbs. In some countries, these materials may be processed by various local procedures, such as steaming, roasting, or stir-baking with honey, alcoholic beverages or other materials (WHO, 2016).

1.3.3 Herbal preparations

The basis for finished herbal products and may include comminuted or powdered herbal materials, or extracts, tinctures and fatty oils of herbal materials. They are produced by extraction, fractionation, purification, concentration, or other physical or biological processes. They also include preparations made by steeping or heating herbal materials in alcoholic beverages and/or honey, or in other materials.

1.3.4 Finished herbal products

Herbal preparations made from one or more herbs. If more than one herb is used, the term mixture herbal product can also be used. Finished herbal products and mixture herbal products may contain excipients in addition to the active ingredients. However, finished products or mixture products to which chemically defined active substances have been added, including synthetic compounds and/or isolated constituents from herbal materials, are not considered to be herbal (WHO, 2016).

The proper and judicious use of herbs is often successful in the treatment of illness when other, more conventional medicines and methods fail. Herbs can be used to cleanse the bowels, open congested sinuses, help mend broken bones, stimulate the brain, increase libido, ease pain, aid digestion, and a thousand other pu rposes. Topically, herbs can repair damaged skin, soothe a wound, improve complexion, heal bruises and relieve aching muscles. Herbs demonstrate great versatility for the treatment of a broad variety of health needs (Medicinehunter, 2014).

1.4 History

1.4.1 Medicinal Plant in Ancient Time

The oldest written evidence of medicinal plants' usage for preparation of drugs has been found on a Sumerian clay slab from Nagpur, approximately 5000 years old. It comprised 12 recipes for drug preparation referring to over 250 various plants, some of them alkaloid such as poppy, henbane, and mandrake.

The Chinese book on roots and grasses "Pen T'Sao," written by Emperor Shen Nung circa 2500 BC, treats 365 drugs (dried parts of medicinal plants), many of which are used even nowadays such as the following: Rhei rhisoma, camphor, Theae folium, Podophyllum, the great yellow gentian, ginseng, jimson weed, cinnamon bark, and ephedra.

The Indian holy books Vedas mention treatment with plants, which are abundant in that country. Numerous spice plants used even today originate from India: nutmeg, pepper, clove, etc. According to data from the Bible and the holy Jewish book the Talmud, during various rituals accompanying a treatment, aromatic plants were utilized such as myrtle and incense.

The works of Hippocrates (459–370 BC) contain 300 medicinal plants classified by physiological action: Wormwood and common centaury (Centaurium umbellatum Gilib) were applied against fever; garlic against intestine parasites; opium, henbane, deadly nightshade, and mandrake were used as narcotics; fragrant hellebore and haselwort as emetics; sea onion, celery, parsley, asparagus, and garlic as diuretics; oak and pomegranate as astringents.

Theophrast (371-287 BC) founded botanical science with his books "De Causis Plantarium"— Plant Etiology and "De Historia Plantarium"—Plant History. In the books, he generated a classification of more than 500 medicinal plants known at the time. Among others, he referred to cinnamon, iris rhizome, false hellebore, mint, pomegranate, cardamom, fragrant hellebore, monkshood, and so forth. In the description of the plant toxic action, Theophrast underscored the important feature for humans to become accustomed to them by a gradual increase of the doses. Owing to his consideration of the said topics, he gained the epithet of "the father of botany," given that he has great merits for the classification and description of medicinal plants.

In his work "De re medica" the renowned medical writer Celsus (25 BC–50 AD) quoted approximately 250 medicinal plants such as aloe, henbane, flax, poppy, pepper, cinnamon, the star gentian, cardamom, false hellebore, etc.

In ancient history, the most prominent writer on plant drugs was Dioscorides, "the father of pharmacognosy," who, as a military physician and pharmacognosist of Nero's Army, studied medicinal plants wherever he travelled with the Roman Army. Circa 77 AD he wrote the work "De Materia Medica." This classical work of ancient history, translated many times, offers plenty of data on the medicinal plants constituting the basic materia medica until the late Middle Ages and the Renaissance (Medknow Publications. 2012).

1.4.2 Medicinal Plant in 21st Century

For centuries people have used plants for healing. Plant products – as parts of foods or botanical potions and powders – have been used with varying success to cure and prevent diseases throughout history. Written records about medicinal plants date back at least 5000 years to the Sumerians (Swerdlow, 2000) and archeological records suggest even earlier use of medicinal plants. The strong historic bond between plants and human health began to unwind in 1897, when Friedrich Bayer and Co. introduced synthetic acetyl salicylic acid (aspirin) to the world. Aspirin is a safer synthetic analogue of salicylic acid, an active ingredient of willow bark, and was discovered independently by residents of both the New and Old worlds as a remedy for aches and fevers (Verpoorte and Alfermann, 2000). The twentieth century became a triumph for the synthetic-chemistrydominated pharmaceutical industry, which replaced natural extracts with synthetic molecules that often had no connection to natural products. The spectacular rise of the pharmaceutical industry had a tremendous impact on disease treatment and prevention, saved countless lives and became one of the outstanding achievements of the twentieth century. However, the benefits of modern drugs are felt primarily in developed countries, and developing countries continue to rely on ethnobotanical remedies as their primary medicines, leaving almost 75% of the world population without access to the modern healthcare products taken for granted in the West. (Raskin, I. *et al.* 2002)

1.4.3 Modern Drug from Medicinal Plant

In present days, almost all pharmacopoeias in the world—Ph Eur 6, USP XXXI, BP 2007— proscribe plant drugs of real medicinal value. There are countries (the United Kingdom, Russia, Germany) that have separate herbal pharmacopoeias. Yet, in practice, a much higher number of unofficial drugs are always used. Their application is grounded on the experiences of popular medicine (traditional or popular medicine) or on the new scientific research and experimental results (conventional medicine). Many medicinal plants are applied through self-medication or at the recommendation of a physician or pharmacist. They are used independently or in combination with synthetic drugs (complementary medicine). For the sake of adequate and successfully applied therapy, knowledge of the precise diagnosis of the illness as well as of medicinal plants, i.e. the pharmacological effect of their components is essential. Plant drugs and phytopreparations, most commonly with defined active components, verified action and, sometimes, therapeutic efficiency, are applied as therapeutic means. In the major European producer and consumer of herbal preparations—Germany, rational phytotherapy is employed, based on applications of preparations whose efficiency depends on the applied dose and identified active components, and their efficiency has been corroborated by experimental and clinical tests. Those preparations have been manufactured from standardized plant drug extracts, and they adhere to all requirements for pharmaceutical quality of drugs.

With the new Law on Drugs and Medical Devices dated September 2007 and enacted in the Republic of Macedonia, dry or sometimes fresh parts of medicinal plants (herbal substances) may be used for preparation of herbal drugs, herbal processed products, and traditional herbal drugs. (Medknow Publications. 2012)

Table 1.1- Some commonly used drugs derived from Plant Sources

Drug/Chemical	Action/Clinical Use	Plant Source
Acetyldigoxin	Cardiotonic	*Digitalis lanata*
Adoniside	Cardiotonic	*Adonis vernalis*
Allyl isothiocyanate	Rubefacient	*Brassica nigra*
Atropine	Anticholinergic	*Atropa belladonna*
Caffeine	CNS stimulant	*Camellia sinensis*
Camphor	Rubefacient	*Cinnamomum camphora*
Demecolcine	Antitumor agent	*Colchicum autumnale*
Digitoxin	Cardiotonic	*Digitalis purpurea*
Ephedrine	Sympathomimetic, antihistamine	*Ephedra sinica*
Hyoscyamine	Anticholinergic	*Hyoscyamus niger*
Papavarine	Smooth muscle relaxant	*Papaver somniferum*
Quinidine	Antiarrhythmic	*Cinchona ledgeriana*
Reserpine	Antihypertensive, tranquillizer	*Rauvolfia serpentina*
Strychnine	CNS stimulant	*Strychnos nux-vomica*

Drug/Chemical	Action/Clinical Use	Plant Source
Taxol	Antitumor agent	*Taxus brevifolia*
Theobromine	Diuretic, vasodilator	*Theobroma cacao*
Thymol	Antifungal (topical)	*Thymus vulgaris*
Vinblastine	Antitumor,Antileukemic agent	*Catharanthus roseus*
Vincristine	Antitumor,Antileukemic agent	*Catharanthus roseus*

(Islam, 2000)

1.5 Future of Medicinal Chemistry

Current research in drug discovery from medicinal plants involves a multifaceted approach combining botanical, phytochemical, biological, and molecular techniques. Medicinal plant drug discovery continues to provide new and important leads against various pharmacological targets including cancer, HIV/AIDS, Alzheimer's, malaria, and pain. Several natural product drugs of plant origin have either recently been introduced to the United States market, including arteether, galantamine, nitisinone, and tiotropium, or are currently involved in late-phase clinical trials. As part of our National Cooperative Drug Discovery Group (NCDDG) research project, numerous compounds from tropical rainforest plant species with potential anticancer activity have been identified. Our group has also isolated several compounds, mainly from edible plant species or plants used as dietary supplements that may act as chemopreventive agents. Although drug discovery from medicinal plants continues to provide an important source of new drug leads, numerous challenges are encountered including the procurement of plant materials, the selection and implementation of appropriate high-throughput screening bioassays, and the scale-up of active compounds (Balunas, M. and Kinghorn, A. 2005).

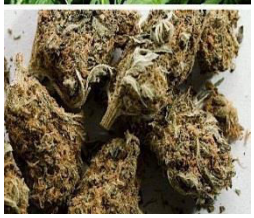
1.6 Economic Opportunities

Medicinal plants play an important role in the development of potent therapeutic agents. During 1950-1970 approximately 100 plants based new drugs were introduced in the USA drug market including deserpidine, reseinnamine, reserpine, vinblastine and vincristine which are derived from higher plants (Sing S.P., 2008). However, the benefits of modern drugs are felt primarily in developed countries, and developing countries continue to rely on ethnobotanical remedies as their primary medicines, leaving almost 75% of the world population without access to the modern healthcare products taken for granted in the West (Verma, S., 2008). It is easy to overlook the fact that human medicines still contain Phytochemicals – valued at US$22 608 million in 1997 and projected to reach a value of US$30 688.5 million in 2002 – with prescription products and over-the-counter (OTC) herbal remedies each comprising approximately 50% of the market (McWilliams, 2014). The severed bond between plants and health was felt not only in the area of medicines. By providing a 'pill option', the pharmaceutical industry also diminished the historical connection between food and the treatment of disease. 'An apple a day keeps the doctor away' is the advice one usually gets from a mother, not from a professional health organization. Plants are slowly making a comeback in several areas of human health (i.e. functional foods, dietary supplements and recombinant protein manufacturing (Raskin *et al*,.2002).

1.7 Medicinal Plants And Their Uses Around The World:

From marijuana to catnip, there are hundreds of remarkably common herbs, flowers, berries and plants that serve all kinds of important medicinal and health purposes that might surprise you: anti-inflammatory, anti-fungal, insect repellent, antiseptic, expectorant, antibacterial, detoxification, fever reduction, antihistamine and pain relief. Here are eighteen potent medical plants:

Table 1.2- Top Medicinal Plants around The World

Plant Names	Description	Uses
1) Marijuana  	It is still illegal in the United States; it is legal in 12 states for medicinal purposes. It is a remarkable and renewable plant, offering all kinds of foodstuff and product uses that surpass cotton and plastic	• Depression and anxiety relief • Reduce blood pressure • Pain alleviation • Glaucoma treatment
2) Blood Flower 	Also called Mexican butterfly weed; is a type of tropical milkweed with toxic milky sap that is emetic.	• Heart stimulant and worm expellent • Pretty useful for a number of potential hiking disasters.
3) Tansy 	It is an old-world aster and remedy, used for flavoring beer and stews as well as repelling insects.	• Effective bug repellent, • treat worms.

Plant Names	Description	Uses
4)Korean Mint 	Most of the various types of "mint" or mentha spearmint,Korean mint, applemint, regular old mint – offer reported health benefits and medicinal properties.	• Soothing headache • Fighting nausea, • Calming the stomach • Reducing nervousness and fatigue. • Useful for fighting colds and the flu.
5) Alfalfa 	Alfalfa is considered the Father of Plants. It's incredibly rich in minerals and health-promoting nutrients and compounds, protein. Alfalfa originally grew in the Mediterranean and Middle East but has now spread to most of Europe and the Americans.	• It can treat morning sickness, nausea, kidney stones, kidney pain and urinary discomfort. • It is a powerful diuretic and has a bit of stimulant power, • It's a liver and bowel cleanser • Long-term can help reduce cholesterol.

Plant Names	Description	Uses
6) Sage 	It grows in the Northern Hemisphere.	• The stems and leaves for healing, • The young shoots peeled as a vegetable of sorts, • Effective treatment against dysentery and diarrhea as well as serving usefulness as an antiinflammatory and astringent. • Ideal for treating cuts and inflammation in the mouth.

Plant Names	Description	Uses
8) Winter savory 	Originally from Europe and the Mediterranean but often shows up elsewhere thanks to global trade.	• It is your savior against insect bites and stings. • In addition to being an antiseptic, • it is delicious – used for flavoring meats and stews.
9) Wild Quinine 	It is a potent herb. Found in eastern native America	• antiperiodic, emmenagogue, kidney, lithontripic, poultice. • traditionally been used in alternative medicine to treat debility, fatigue, respiratory infection, gastrointestinal infection, and venereal disease.
10) Blackberries 	Found widely in native America	• Antioxidants and vitamins, • stems and leaves for healing, • effective treatment against dysentery and diarrhea • usefulness as an anti-inflammatory and astringent. • treating cuts and inflammation in the mouth.

1.8 Medicinal Plants In India

India is rich in culture. We have had different human advancements that have added to making this land flourish. There have been numerous who have come, bestowed intelligence identified with different points and have helped us as a human race to develop and advance. Without our current mechanical progressions, we have checked and cured various diseases and sicknesses with the assistance of therapeutic plants and home grown cures.

An Ayurvedic form of medicine is believed to be existent in India for thousands of years. It employs various techniques and things to provide healing or relief to the ailing patients. One of the things that Ayurveda uses is medications of plant origin.

It is very important to have medicinal plants around the house cause you never know when you might need them. So here a list of medicinal plants that have the highest medicinal value compared to the other million species around the world worth planting around the house.

Table 1.3- Medicinal Plants Used In India

Plant Name	Description	Uses
1) Tulsi	**For over the centuries Tulsi, known as the queen of herbs has been known for its remarkable healing properties. The fresh leaves of Tulsi are taken by the millions of people every day.**	• **Taken as the herbal tea.** • **Tulsi oil is also used as the ear drop.** • **Tulsi helps in curing malaria. It is very effective against indigestion, headache, hysteria, insomnia and cholera.** • **The Rama Tulsi is the effective remedy for the severe acute Respiratory Syndrome.**

2) Aloe Vera	Aloe Vera grows only under the sun with well drained, dry or moist soil. Although this Ayurvedic plant tastes very bad, it's still edible.	• Speed up the healing reduce the risk of infections of various things like wounds cuts burns and even reduces inflammation • Ulcerative colitis • Chronic constipation • Poor appetite • Digestive problems
3) Basil	It must be used many times in our food.	• Cuts • Lack of appetite • Stomach gas • Scrapes
4)Rosemary	A row of these long-lived and drought-tolerant plants makes a beautiful, bee-friendly, evergreen hedge. You may only need one plant in your garden, as a little bit goes a long way.	• Rosemary is the great reviver. • This perennial woody herb stimulates energy and optimism and sharpens memory and concentration by bringing more oxygen to the brain. • It's a wonderfully stimulating alternative to caffeine.

5) Lavender	Long recognized for its sweet perfume, Lavender also boasts medical benefits as a nerving and mild antidepressant. Adding to bath alleviates stress, tension, and insomnia.	• It's also used in creams to treat sunburns and acne. • Woody lavender plants prefer hot, sunny, and dry environments. • The fresh flowers are tasty in small doses when added to salads, honey, butter, lemonade, and even shortbread cookies.
6)Fenugreek, Methi	It is cultivated worldwide as a semiarid crop, and its seeds are a common ingredient in dishes from the Indian subcontinent.	• Fenugreek seeds are nourishing and taken to encourage weight gain • Inhibit cancer of the liver, lower blood cholesterol levels, • Treat inflammation and ulcers of the stomach and intestines, • Drain off sweat ducts, for late onset diabetes, • Helps poor digestion, • Painful menstruation, • Labor pains, • Freshen bad breath and restores a dull sense of taste.

7)Peppermint:	Peppermint is sometimes regarded as 'the world's oldest medicine', with archaeological evidence placing its use at least as far back as ten thousand years ago. Peppermint is naturally high in manganese, vitamin A and vitamin C.	• Crushed leaves rubbed on the skin help soothe and relax the muscles • Reduce irritable bower syndrome • Against upset stomachs • Inhibit bacterial growth • Treat fevers • Flatulence • Spastic colon

(Ayushakti,2016)

1.9 Medicinal Plants In Bangladesh

In an estimate, the international market of medicinal plants related to trade stood at 60 billion US Dollar per year. The demand for medicinal plants based raw materials are growing at an approximate rate of 10-15% per year internationally. Medicinal plant sector has traditionally occupied an important position in the socio-cultural, spiritual and medicinal arena of rural and tribal lives of Bangladesh. In recent years, the growing demand for herbal product has led to a quantum jumping in volume of plants materials trade within and across the country. In Bangladesh there are no systematic cultivation process or conservation strategies about medicinal plants. The local people conserve traditional knowledge through their experience and practice, which is handed down orally without any documentation. This knowledge is now under threat to extinction. This is a very alarming situation with regard to natural growth of medicinal plants in the wilderness in this country. In a survey on "Traditional and industrial use and market

Scenario of Medicinal plants in Bangladesh." conducted by the DEBTEC researchers at Chakbazar, Dhaka, Bangladesh, found that there is worth of 11 million US dollars medicinal plant market in Bangladesh, which have been imported but not in the name of medicinal plants rather in the name of spices and other products. Another research

aimed at documenting the 'Present Status and Market Scenario of Medicinal Plants' in Bangladesh shows that 84.1% of the respondent use medicinal plants in health care. 18.3% of the villagers use Kabirazi in the disease in medium category. 55.0% of respondent's source of knowledge of using medicinal plant is family where 34.7% gained knowledge from neighbor. Only 14.3% of the respondents are involved with trading of medicinal plant. About 10.4% of the villagers are involved in cultivation, collection or business of medicinal plant. From the survey report it has been found that 46.6% industries are using above 60% of imported medicinal plants as their raw materials and 53.3% of the industries are using below 40%. The study revealed that 86.7% industries are importing Indian raw materials, 53.3% are importing the Pakistani one and very few of them are importing the raw materials from Nepal, Iran and Korea. According to the response of shop owners, the local raw materials of their products are mostly coming from 5 different areas of the country. Among those 90% are coming from Chittagong and again 76.6% from Tangail, 30% from Gazipur and another 30% from Khulna (Mpbd.info, 2014).

Table 1.4- Medicinal plant species listed by WHO which can be grown in Bangladesh commercially

Scientific name	Bengali name	English name	Used parts	Used as patent drugs
***Winthania somnifera* Dunal**	Ashwagandha	Winter Cherry	Root, Leaf, Fruit, Seed, whole plant	Syrup Masturin, Arq Ashwaganda. Magun Sohag Soonth
***Aloe vera* Tour. ex Linn.**	Ghritokumari	Aloe	Leaf	Tablet Suranjan, Tablet Mudir, Syrup Belgiri
***Andrographis panniculata*Wall.ex Nees.**	Kalomegh	Creat	Leaf, Stem, whole plant	Syrup Safi, Syrup Kurchi
***Asparagus racemosus* Willd.**	Satomuli	Asparagus	Tuberous root, Leaf, Flower, Fruit	Tablet Abiaj, Khisandha, Ka-4, Sufoof Gigian
***Plumbago zeylanica* Linn.**	Chita		Root	Majoon Falasefa, Syrup Kurchi

***Adhatoda zeylanica* Nees. (Syn. name- *A. vasica* Linn.)**	Vasak	Vasaka	Leaf, Stem, Bark, Root, Flower	Syrup Saduri, Chawan Prash, Tablet Sualin, Syrup Ajaj
***Rauvolfia serpentine* (Linn.) Benth.**	Swarpagandha	Snake root	Root	Syrup Mangurin
***Glycyrrhiza glabra* Linn.**	Jastimodhu	Liqouric e root	Root, Stem	Tablet Sualin, Mauol Hiat, Syrup Badian, Tablet Kafur

(Islam *et al* ,2003)

1.10 Synthetic Medicine

A synthetic medicine is a medicine with properties and effects similar to a known hallucinogen or narcotic but having slightly altered chemical structure, especially Such a drug created in order to evade restrictions against illegal subtances.

Examples of synthetic drugs are synthetic phenethylamines, including synthetic cathinones or synthetic hallucinogens and, more commonly known as “bath salts”. Synthetic cannabinoids, also known as synthetic marijuana, are another example of designer drugs and these are often found in herbal incense products that mimic the effects of delta-9-tetrahydrocannabinol (THC), the primary psychoactive constituent of marijuana (New York State Department of Health, 2012).

1.10.1 Disadvantages of Synthetic Medicine

The new synthetic drugs that are making the rounds of drug-using markets are some of the most destructive drugs available today. Older drugs like heroin and cocaine could destroy a person's life by causing a general deterioration of quality of life or by overdose, but many of these new drugs can destroy a life by triggering psychotic episodes of hallucinations, aggression, paranoia, suicidal thoughts or impulses and homicidal tendencies.

LSD, PCP and Ecstasy (MDMA) were the earlier synthetic drugs and amphetamine and methamphetamine were even earlier than that. Now, international chemists seem to have discovered this new market and are distributing one new destructive chemical after another into the illicit drug market. Some of them manage to stay one step ahead of the law by shifting the formula of a particular drug they are selling, as soon as it has become illegal. They just move a few molecules and they have a new chemical that may not be illegal (Marconon, 2016).

The adverse effects of these drugs go far beyond the idea of the overdose, suppressed breathing or slowed heart rate of more common drugs. The effects of these synthetics can be so violent as to take out not only the drug user himself (or herself) but also children or adults in the vicinity.

One example of synthetic marijuana is sold as Spice or K2 or one of a dozen other names. It produces some effects similar to marijuana but much stronger and with a faster onset. Some people use this drug because it could not be detected on a drug test, but this is no longer true. Other people used it because it was not illegal, but that is not true now either (Marconon, 2016).

Some users have experienced severe episodes of psychotic behavior. Paranoia, extreme anxiety and hallucinations can result in aggressive, even homicidal behavior. Compounds used in Spice have also caused rapid heart rate, increased blood pressure, vomiting and confusion. It has also been associated with heart attacks.

There's another set of chemicals that are sold as "bath salts." These drugs are packaged in small foil envelopes that say "for a refreshing bath, not for human consumption." These packets may contain mephedrone, MDPV (methylenedioxy pryrovalerone) or any of eighty other chemicals. Bath salts are supposed to mimic the effects of cocaine or methamphetamine. Use of these drugs may also result in paranoia, violent behavior, higher blood pressure and possible heart attack or stroke. Paranoia and violent, aggressive tendencies have resulted in assaults, murders and suicides (Marconon,2016).

There are some drugs that are only known by a letter-number combination, like 2C-I or 2C-B. In Australia, fatal effects have resulted from a synthetic known only as 25B-NBOMe. These drugs were distributed on small fragments of paper, like LSD has been. Effects like bizarre behavior, paranoia and confusion have been seen after use of this drug as well.

Moreover, addiction makes these drugs particularly dangerous.because all these drugs are addictive, a person may start using them, suffer terrible damage and not be able to stop himself (or herself) from going back to them again and again. When addiction threatens a person's life in this way, he must have access to a drug rehabilitation program that helps him build a new, sober life. With drugs this heavy, it takes a thorough program that teaches new life skills and that allows for deep detoxification of drug residues that might continue to affect mood (Marconon, 2016).

1.11 Studying Herbal Medicine

Herbal medicine remains largely an unproven, inexact science. Although the history of herbal medicine provides decades, sometimes centuries, of anecdotal information, scientific study of herbal medicine is relatively new. The U.S. Department of Health and Human Service's National Center for Complementary and Alternative Medicine (NCCAM) has only been in operation since 1992. Compared to the Federal Food and Drug Administration (FDA), which was founded over 100 years ago, NCCAM has only begun to scratch the surface of scientific research (Jeanne. 2014).

Despite the criticism of herbal medicine among mainstream medical professionals, it is wise to remember that many common drugs we use today were derived from plant-based sources. For example, scientists originally derived aspirin from willow bark; herbalists prescribe white willow for headaches and pain control. Digitalis, a drug prescribed for certain heart conditions, comes from an extract of potentially toxic foxglove flowers (Jeanne G.,2014). These are just a few examples of why it's important studying herbal medicine but without significant scientific study it is not safe of using herbal medicine as treatment of any disease. Because, herbs are not without disadvantages, and herbal medicine is not appropriate in all situations. These are a few of the disadvantages to consider:

- **Inappropriate for many conditions-** would not be able to treat serious trauma, such as a broken leg, nor would he be able to heal an appendicitis or a heart attack as effectively as a conventional doctor using modern diagnostic tests, surgery, and drugs (Jeanne, 2014 and MedicinePlus, 2016).
- **Lack of dosage instructions-** may cause accidentally overdosing on cold remedies, many herbs do not come with instructions or package inserts. There's a very real risk of overdose.
- **Poison risk associated with wild herbs**- Harvesting herbs in the wild is risky, if not foolhardy, yet some people try to identify and pick wild herbs. (Jeanne, 2014 and MedicinePlus, 2016).
- **Medication interactions**- Herbal treatments can interact with medications. Nearly all herbs come with some warning, and many, like the herbs used for anxiety such as Valerian and St. John's Wort, can interact with prescription medication like antidepressants (Jeanne, 2014 and MedicinePlus, 2016).
- **Lack of regulation-** Because herbal products are not tightly regulated, the quality of herbal products may vary among batches, brands or manufacturers. This can make it much more difficult to prescribe the proper dose of an herb (Jeanne, 2014).

The bottom line is that herbs are medicines, and like other medications, though they have some disadvantages. With proper scientific investigation we can make the best use of our natural products (Jeanne., 2014).

1.12 Reasons Behind Physicochemical Investigations

The importance of medicinal plants, are extremely useful for us on the one hand they provide us with the oxygen we need to be able to breathe for edible landscaping. The most important of these bioactive constituents of plants are alkaloids, tannins, flavondoids, and phenolic compounds. Many of these indigenous medicinal plants are used as spices and food plants. They are also sometimes added to foods meant for pregnant and nursing mothers for medicinal purposes. Traditional knowledge of medicinal plants has always guided the search for new-cures. In spite of the advent of modern high throughout drug discovery and screening techniques. Traditional knowledge systems have given clues to the discovery of valuable drugs (Belay and Sesay, 2014).

The World health organization (WHO) estimates that 4 billion people (80%) of the world's population presently use herbal medicine for one form of primary health care or another. Its history is inextricably intertwined with that of modem medicine, but pharmacologists, rather than use a whole plant identify, isolate, extract and synthesize individual components, thus capturing the active properties as against the herbalist who considers that the power of a plant lies in the interaction of all its ingredients .

Herbal medicines are promising choice over modern synthetic drugs. They show minimum or no side effects and are considered to be safe. Generally herbal formulations involve the use of fresh or dried plant parts. Correct knowledge of such crude drugs is very important aspect in preparation, safety and efficacy of the herbal product.

Pharmacognosy is a simple and reliable tool, by which complete information of the crude drug can be obtained . Medicinal plants are of great importance to the health of individuals and communities. The medicinal value of these plants lies in some chemical substances that produce a definite physiological action on the human body. Many of these indigenous medicinal plants are used as spices and food.

Medicinal herb is considered to be a chemical factory as it contains a multitude of chemical compounds like alkaloids, glycosides, saponins, resins, oleoresins, sesquiterpene, locations and oils (essentialand fixed) . Higher plants produce both primary and secondary chemical metabolites, the former being vitally important in normal development and reproduction of plants. On the other hand, secondary metabolites are known to play important roles in plant survival as defense mechanisms against adverse biotic and a biotic conditions . Extraction (as the term is pharmaceutically used) is the separation of medicinally active portion of plant (and animal) tissue using selective solvents through standard procedures.

The products so obtained from plants or semisolid state or (after removing the solvent) in dry powder form, and are intended for oral or external use, these include classes of preparations know as decoctions, infusions, fluid extracts, tinctures, pillar (semi solid) extracts or powdered extracts .

The purpose of standardized extraction procedures for crude drugs (medicinal plant parts) is to attain the therapeutically desired portions and to eliminate unwanted material by treatment with a selective solvent known as menstruum. The extract thus obtained, after standardization, may be used as a medicinal agent as such in the form of tinctures or fluid extracts or further processed to be incorporated in any dosage form such as tablets and capsules. These products contain a complex mixture of many medicinal plant metabolites, such as alkaloids, glycosides, terpenoids, Flavonoids and lignans. (Ahmad *et al.*, 2013)

1.13 Significances of Medicinal Plants to Human Being

- Many of the modern medicines are produced indirectly from medicinal plants, for example aspirin.
- Plants are directly used as medicines by a majority of cultures around the world, for example Chinese medicine and Indian medicine.
- Many food crops have medicinal effects, for example garlic.
- Medicinal plants are resources of new drugs. It is estimated there are more than 250, 000 flower plant species.
- Studying medicinal plants helps to understand plant toxicity and protect human and animals from natural poisons.
- Cultivation and preservation of medicinal plants protect biological diversity, for example metabolic engineering of plants.

(cals.ncsu, 2016)

1.14 Importance of Medicinal Plant

Before onset of synthetic era, man was completely dependent on medicinal herbs for prevention and treatment of diseases. With introduction of scientific procedures the researchers, were able to understand about toxic principles present in the green flora. The scientists isolated active constituents of the medicinal herbs and after testing some were found to be therapeutically active. Aconitine, Atisine, Lobeline, Nicotine, Strychnine, Digoxin, Atropine, Morphine are some common examples.

While medicinal plants are the actual plants themselves, plant medicines are preparations made from those plants. Plant medicines are the most widely used medicines in the world today. An estimated eighty percent (80%) of the world's population employs herbs as primary medicines. And while drugstore shelves in the US are stocked mostly with synthetic remedies, in other parts of the world the situation is quite different. In parts of Europe, for example, pharmacies dispense herbs prescribed by physicians.

For 5.1 billion people worldwide, natural plant-based remedies are used for both acute and chronic health problems, from treating common colds to controlling blood pressure and cholesterol. Not so long ago, this was true in the US as well. As late as the early 1950's, many of the larger pharmaceutical companies still offered a broad variety of plant-based drugs in tablet, liquid and ointment forms.

The efficacy of some herbal products is beyond doubt, the most recent examples being Silybum marianum (silymarin), Artemisia annua (artemesinin) and Taxus baccata (taxol). On the other hand, randomized, controlled trials have proved the efficacy of some established remedies, for instance, Ginkgo biloba for tinnitus, Hypericum perforatum is a reputed remedy for depression. In Hypericum some researchers are of the view that hypericin is the active principle of the herb and some believe that hyperforin is responsible for antidepressant action of the herb.

Recently research has supported biological activities of some medicinal herbs. Cancer is such a segment where researchers are expecting new molecules from herbs that can provide us with tools for fighting this dreaded disease. Allamanda cathratica [allamandin], Elephatopus elatus [elephantpoin], Helenium autmnale [helenalin] Vernonia hymenlepis,

Heliotropium indicum [Indicine-N-oxide], Daphne mezereum (mezerien) and Stereospermum suaveolans [laphacol] are medicinal plants that have shown significant tumor inhibiting effect (Medicinehunter. 2014; Worldpress. 2015).

1.15 Plant Review:

1.15.1 Plant Name: *Stereospermum cheloniedes*

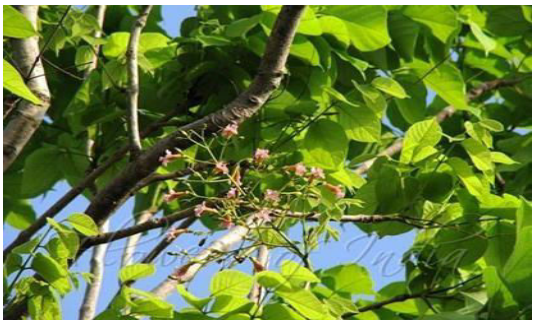


Figure 1.1 ***Stereospermum cheloniedes***

1.15.2 Description: Fragrant Padri Tree is a large deciduous tree, 10-20 m tall, with velvet-hairy branches. Leaves are compound, 1-2 ft long, with 3-4 pairs of leaflets. Leaflets are 7-15 cm long, broadly elliptic, long-pointed. velvety on the underside, rounded and unequal at base, with 6-8 nerves, short-stalked. Fragrant flowers are borne in large lax panicles. They are 10-20 cm long, pinkish. Sepal cup is bell-shaped, 1 cm long, hairy, 3-5 lobed. Stamens are 4, remaining inside the flower-tube. Seed-pod is 1-2 ft long, cylindric, ribbed, rough. The Tree is globally distributed in Indo-Malesia. Within India, it is found in tropical Himalayas, Assam, Meghalaya and in moist deciduous forests of Western Ghats.

(Shrikant,2016)

1.15.3 Classification:

Kingdom- Plantae

Phylum . Tracheophyta

Class - Magnoliopsida

Order - Lamiales

Family – Bignoniaceae

Genus - *Stereospermum*

Species - *Stereospermum chelonoides* (L. fil.) DC.

Synonyms: *Bignonia chelonoides, Bignonia suaveolens, Stereospermum suaveolens* (Biodiversity, 2016).

1.15.4 Vernacular Names Of Plant:

Bangla/Vernacular	Dharmara(Chittagong),Barul-jata,Atkapali,Pahari Awal (Sylhet)
English	Rose Flower Fragrant , Bignonia suaveolens
Assamese	Parhori, paroli, ser phang
Garo	Bolsel
Hindi	Padeli
Kannada	Adri,bili paadri, giri, hadar
Khasi	Dieng sir
Malayalam	kacasthali, karannavu, karanyavu
Mizo	Zinghal
Naga	Ing-nge-ching
Nepali	Kuber bacha, jinghal, parhori
Sanskrit	kastapatala, patala
Tamil	ambuvagina, padiri, pathiriver, pumbadir
Telugu	ambuvaasini,gallugudu, goddalipukusu, isakarasi.

(ShrIkant, 2016)

1.15..5 Tribal Name: Hamarang gaas (Chakma), Chain-cha (Marma), Sekwai (Chakma), Goda-kamarang (Mogh), Batsil (Garo), Bol-sal (Garo).
(ShrIkant. 2016)

1.15.6 Profile of *Stereospermum chelonoides*

Seed Number	Numerous
Disk Texture	Fleshy
Seed endosperm	Absent
Staminode Number	1, 2, and 3
Root Type	Taproot system
Leaf Venation	Reticulate or net Veined
Sexuality	Bisexual
Perianth Aestivation	Imbricate or valvate (Corolla)
Locule Number	2- locular, rarely 1 - or 4 - locular
Placentation	Axile or parietal
Inflorescence Parts	Bracts, bractlets, flowers
Fruit Type	Capsule , Loculicidal or septicidal, rarely indehiscent
Stem Appendages	tendrils modified somtimes into hooks or suckers (in Climbers)
Leaf Arrangement	Opposite, alternate, or whorled
Stamen N	4(fertile stamens)
Ovule Number	Numerous
Stipule Presence or Absence	Absent
Stigma structure	2 – lobed

(Species Directory, 2016)

1.15.7 Bignoniaceae family:

1.15.7.1 Habit and leaf form: Trees, or shrubs, or lianas, or herbs (rarely). Self-supporting, or climbing; when climbing stem twiners, or tendril climbers (via modified terminal leaflets), or root climbers; the twiners twining anticlockwise (Tecoma). Leaves opposite (mostly), or whorled, or alternate (rarely, then spiral); petiolate; non-sheathing; compound (usually), or simple; pinnate, or palmate, or bipinnate, or multiply compound. Lamina when simple dissected, or entire; when dissected pinnatifid, or palmatifid. Leaves exstipulate; leaf development not 'graminaceous'. Domatia occurring in the family (known from 14 genera); manifested as pits (rarely), or pockets, or hair tufts.

1.15.7.2 Leaf anatomy:

Figure 1.2 Leaves of *Stereospermum chelonoides*

The leaf lamina dorsiventral (usually), or bifacial (isobilateral recorded in Kigelia). Stomata present; nearly always mainly confined to one surface (abaxial); anomocytic, or paracytic, or diacytic (Kigelia). Adaxial hypodermis present (rarely, e.g. in Pandorea), or absent. The mesophyll with sclerenchymatous idioblasts (spicular cells), or without sclerenchymatous idioblasts; containing crystals. The crystals mostly solitaryprismatic (in the form of small octahedra, prisms or needles: large solitary crystals and druses rare). Minor leaf veins without phloem transfer cells (Catalpa, Jacaranda, Tecomella).

1.15.7.3 Axial (stem, wood) anatomy: Cork cambium present; initially deep-seated, or initially superficial. Nodes unilacunar (3 to several traces). Primary vascular tissues in a cylinder, without separate bundles. Internal phloem absent. Cortical bundles absent. Medullary bundles present (these inversely orientated, e.g. in Campsis, Tecoma), or absent. Secondary thickening developing from a conventional cambial ring, or anomalous (represented by assorted variations, featured in Solereder's generic key). The anomalous secondary thickening via concentric cambia (e.g. Campsis, Clytostoma, Tecomaria, where a second series of bundles forms internally to the primary cylinder, in the pith; or in the secondary cortex), or from a single cambial ring. Primary medullary rays wide (in lianes), or mixed wide and narrow.

The wood variously ring porous, or semi-ring porous, or diffuse porous. The vessels small, or medium (mostly), or large. The vessel end-walls simple (typically), or reticulately perforated and simple. The vessels without vestured pits; with spiral thickening, or without spiral thickening. The axial xylem without fibre tracheids; with libriform fibres; including septate fibres (commonly, especially in climbers), or without septate fibres. The fibres without spiral thickening. The parenchyma paratracheal. The secondary phloem stratified into hard (fibrous) and soft (parenchymatous) zones (commonly), or not stratified. 'Included' phloem present (as wedges in the xylem), or absent. Reproductive type, pollination. Plants hermaphrodite. Pollination entomophilous, or ornithophilous, or cheiropterophilous (Watson & Dallwitz, 1992).

1.15.7.4 Inflorescence, floral, fruit and seed morphology: Flowers solitary, or aggregated in 'inflorescences'; when aggregated, in cymes, or in racemes. The ultimate inflorescence units cymose, or racemose. Inflorescences terminal, or axillary; usually dichasial, tending to cincinnial. Flowers somewhat irregular to very irregular. The floral irregularity involving the perianth and involving the androecium (K irregular, C sometimes more or less regular). Flowers more or less 5 merous; cyclic; tetracyclic. Hypogynous disk usually present.

1.15.7.5 Perianth with distinct calyx and corolla: 10; 2 whorled; isomerous. Calyx 5; 1 whorled; gamosepalous; entire, or toothed; campanulate; unequal but not bilabiate, or bilabiate; often open in bud. Corolla 5; 1 whorled; gamopetalous. Corolla lobes markedly shorter than the tube, or about the same length as the tube. Corolla imbricate, or valvate (rarely); usually campanulate, or funnel-shaped; bilabiate (often, the upper lip with two lobes, the lower with three), or regular (rarely).

1.15.7.6 Gynoecium 2 carpelled: The pistil 1 celled, or 2 celled, or 4 celled. Gynoecium syncarpous; synovarious to synstylovarious; superior. Ovary 1 locular, or 2 locular, or 4 locular. Locules secondarily divided by 'false septa', or without 'false septa'. Gynoecium median; stylate. Styles 1; attenuate from the ovary; apical. Stigmas 1; 2 lobed; wet type; papillate; Group III type. Placentation when unilocular parietal; when 2 or 4 locular axile. Ovules in the single cavity when unilocular, 6–100 (to 'many'); 6–50 per locule ('many'); ascending; orthotropous, or hemianatropous; unitegmic; tenuinucellate. Endothelium differentiated. Embryo-sac development Polygonum-type. Polar nuclei fusing prior to fertilization. Antipodal cells formed; 3; not proliferating; ephemeral to persistent. Synergids hooked (large). Hypostase usually present (but weak). Endosperm formation cellular. Endosperm haustoria present; chalazal, or chalazal and micropylar (Watson & Dallwitz, 1992).

1.15.7.7 Fruit: non-fleshy (usually), or fleshy (rarely); dehiscent (usually), or indehiscent (rarely); a capsule (usually), or a berry (rarely). Capsules septicidal, or loculicidal. Seeds nonendospermic (with Schlegelieae excluded); winged (usually), or wingless. Cotyledons 2; flat (enlarged, foliaceous). Embryo achlorophyllous (4/4); straight. Seedling. Germination phanerocotylar, or cryptocotylar.

1.15.7.8 Physiology, phytochemistry: C3. C3 physiology recorded directly in Catalpa, Chilopsis. Sugars transported as oligosaccharides + sucrose (predominantly), or as sugar alcohols + oligosaccharides + sucrose. Not cyanogenic. Alkaloids present, or absent. Anthraquinones detected (4 genera); derived from shikimic acid. Verbascosides detected (8 genera). Cornoside detected (Eccremocarpus). Arbutin absent. Iridoids detected (very commonly); 'Route I' type (normal, doubtfully), or 'Route II' type (normal and decarb.). Saponins/sapogenins present (rarely), or absent. Proanthocyanidins absent. Flavonols present, or absent; when present, quercetin.

Ellagic acid absent (8 species, 7 genera). Ursolic acid present. Aluminium accumulation not found.

1.15.7.9 Special distinguishing feature: The funicles not as in Acanthaceae.

1.15.7.10 Geography, cytology: Temperate (a few), or sub-tropical and tropical (mainly). Widespread, with Catalpa common to the Old and New Worlds. N = 20 (mostly). Supposed basic chromosome number of family: 7 (Watson & Dallwitz, 1992).

1.15.8 Cultivation Details:

A plant of the moist subtropics and tropics, where it is found at elevations up to 1,300 metres. It grows best in areas where annual daytime temperatures are within the range 24 - 32°c, but can tolerate 5 - 47°c. When dormant, the plant can survive temperatures down to about -5°c, but young growth can be severely damaged at -1°c. It prefers a mean annual rainfall in the range 1,200 - 2,500mm, but tolerates 750 - 3,800mm. Grows best in a sunny position, tolerating light shade. Succeeds in a wide range of well-drained soils. Prefers a pH in the range 6 - 7, tolerating 5.5 - 7.5. The tree sometimes suckers very freely.Trees can survive forest fires. It is one of the commonest trees to be seen in the savannah lands of India, apparently able to shoot up yearly in spite of fire, and to grow on into a tree if only a short period of immunity from fire can be obtained. The tree regenerates very freely from seed in the wild. (ken, 2014)

1.15.9 Uses:

Edible Uses: Tender young fruit - cooked and eaten as a vegetable.

Flowers - cooked and used as a vegetable.

1.15.9.1 Traditional uses:

It has been found that the root and bark have medicinal beefits. Traditionally, the decoction of bark and root is used for the treatment of many diseases.

- The chemical lapachol present in it can prevent cancer.
- The decotion made from the roots given to the patients of rheumatoids,
- The ash got from the burning of the roots and barks mixed with water can be used to treat blockage in urinary tract,
- The flowers ontain carbohydrates and fats,
- The flowers are mixed with honey and given orally, for the control of hiccup,
- In southern India, the bark is used traditionally for the treatment of diabetes.
- The fruit is useful for the treatment of leprosy,
- The root has an anticancer activity and also used in preparation of Ayurvedic formulation known as Dashmula. (Insadreams, 2016).

It can be also used to treat:

- pain,
- fever,
- inflammations,
- asthma,
- liver disorders,
- acidity and
- as a diuretic. (Balasubramanian *et al.*, 2012) (Insadreams, 2016)

1.15.9.2 Other Uses

The grey wood is hard, elastic, moderately durable, easy to work. Usually there is no heartwood. It is used for making furniture, construction, tea boxes, canoes etc. An excellent fuel, the wood also makes a good charcoal. (Ken, 2014)

1.16 Study Design

For the treatment of new diseases and the existence diseases, different drugs are required as well as also identified. We have noticed that human body have become resistant to drugs which are available in market. Also because of using synthetic drugs, various toxic and side effects occur. So recently, curiosity has grown in world for herbal medicines which are obtained from medicinal plant. So we have selected *Stereospermum chelonoides* leaves for study because of its medicinal uses.

Analgesic drug means that relieves pain selectively without blocking the conduction of nerve impulses, markedly altering sensory perception, or affecting consciousness. This selectivity is an important distinction between an analgesic and an anesthetic. Analgesics may be classified into two types: anti-inflammatory drugs, which alleviate pain by reducing local inflammatory responses; and the opioids, which act on the brain. The opioid analgesics were once called narcotic drugs because they can induce sleep. The opioid analgesics can be used for either short-term or long-term relief of severe pain. In contrast, the anti-inflammatory compounds are used for short-term pain relief (EncyclopediaBritanica, 2016).

But these both can cause adverse effects which are very common but yet these drugs are very important to our day to day life. So, investigation in producing more and more analgesic drug is needed like in this research *Stereospermum chelonoides* (leaves) was selected to investigate its analgesic activity. If elimination of poisonous compound is possible from this plant, then this experimental plant can be used for the treatment of various diseases.

1.17 Objective

In order to achieve these aims, the following research objectives have been identified:

- To determine the analgesic activity by acetic induced writhing test.

Chapter: 2

Literature & Review

2.1 Chemical Constituents

It was found from a research work with the leaves of *Stereospermum chelonoides* contain flavones glycoside 6-O-glucosylscutellarein, dinatin, dinatin-7glucuroniside,dinatin 7-glucuronide, quinones, stereochenols A and B, naphthoquinones, sterekunthal B and sterequinone C,stereolensin, p-coumaric acid, palmitic, stearic and oleic acids. previously been reported from this plant.

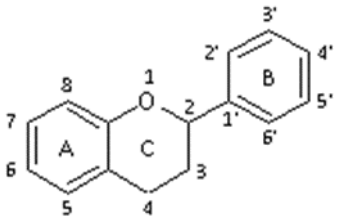


Fig 2.1 Basic Structure of Flavonoides

It was also been reported that plants of the genus *sterepspermum* contains naphthaquinone, lapachol, root bark contains β-sitosterol, n-triacontanol, root heart wood contains lapachol, dehydro-α-lapachone and dehydrotectol. (Mohammmad *et al,* 2006)

In another study fresh and market roots of drug *Stereospermum chelonoides* DC. were analyzed for study in changes of chemical constituents under storage. Root samples were stored under different 30, 50, 75, 96 and 100 % relative humidity and different incubation days 15, 30, 45 and 60 days. Quantitative estimation of carbohydrates, proteins and phenols in fresh and market roots was done. The results indicated that biodeterioration of selected chemical constituents were observed under high relative humidities 75, 96 and 100% RH and with increased incubation days (45 and 60). More deterioration of chemical constituents recorded in case of market samples as compared to fresh samples. Analysis of variance also showed that the effect of relative humidity and incubation days on biodeterioration of chemical constituents amount were significant. (Masoumeh, 2013)

2.2 Secondary Metabolites

Five compounds namely, sterekunthal B (1), sterequinone C (2), p-hydroxybenzaldehyde (3), p-hydroxyphenylmethyl ketone (4) and stigmasterol (5) were isolated from methanolic extract of the stem bark of Stereospermum chelonoides. The structures of compounds 1-5 were established by extensive spectroscopic studies, notably high field NMR and MS. This is the first report of occurrence of 1-5 from *Stereospermum chelonoides*. (Mohammad *et al*, 2006)

2.3 Antioxidant and Anti-Cancer Activity

It was found from a research study that *Stereospermum chelonoides* contains phytochemicals comprising of phenols and flavonoids have cancer prevention agent properties, in the long run renders a lucrative apparatus to search receptive oxygen species (ROS). Along these lines, different in vitro measure methodologies were executed to assess cancer prevention agent capability of Stereospermum chelonoides, utilizing DPPH (1,1-diphenyl-2-picrylhydrazyl) searching test, ferric decreasing cell reinforcement control (FRAP), add up to cell reinforcement limit, assurance of aggregate phenol and flavonoid substance. The IC_{50} estimation of the rough methanol concentrate of bark and leaf was 53.99±3.25 µg/mL and 84.73±4.02 µg/mL, individually, while IC_{50} esteem for the reference ascorbic corrosive was 14.56±0.24 µg/mL. Additionally, significant aggregate cancer prevention agent movement was watched for bark (309.88±1.03 mg/g proportionate to ascorbic corrosive) and leaf (147.09±1.79 mg/g identical to ascorbic corrosive) at 200 µg/mL remove focus. Moreover, extricate indicated great lessening power capacity in both bark and leaf division. Add up to phenol content for the bark was 574.82 mg/g identical to gallic corrosive and for leaf was 189.86 mg/g. For bark, the aggregate flavonoid substance was discovered 55.82 mg/g comparable to quercetin and for leaf it was 49.44 mg/g. (Meena *et al.,* 2013)

2.4 Antimicrobial and Cytotoxic activities

This research report the antimicrobial and cytotoxic activities of the extracts of *S. chelonoides*. Extraction of dried powdered stem bark of S. chelonoides with methanol and subsequent Kupchan partitioning gave n-hexane and chloroform soluble fractions which showed significant cytotoxic activity against brine shrimp nauplii and the LC_{50} values for them were found to be 0.98 and 1.00 µg/ml, respectively. An approximate linear correlation was observed when logarithm of concentration versus percentage of mortality was plotted on the graph paper and the values of LC50 were calculated using Microsoft Excel 2000. All the values were compared with vincristine sulphate whose LC_{50} was found to be 0.33 µg/ml (Mohammad et al, 2006) .

2.5 Hepatoprotective activity

The present study intends to assess the hepatoprotective action on via carbon tetrachloride (CCl4)- instigated liver harm in pale skinned person rats. Biochemical parameters, for example, serum glutamate oxaloacetate transaminase (SGOT), serum glutamate pyruvate transaminase (SGPT), antacid phosphatase (ALP), add up to bilirubin, LDL-cholesterol and SOD, CAT, GSH, add up to thiols, NO, and lipid peroxidation in liver tissue homogenate were used.. The outcomes propose that the methanol stem bark concentrate of the plant at the dosages 125, 250, and 500 mg/kg and reference standard Liv-52 treated gathering created huge ($p < 0.001$) hepatoprotection against CCl4-initiated liver harm by diminishing the exercises of serum proteins, bilirubin and lipid peroxidation. The concentrate fundamentally ($p < 0.001$) expanded levels of SOD, CAT, GSH and add up to thiols, when contrasted with control amass (V.M. CHandrashekhar et al, 2010).

Chapter: 3

Materials & Methods

3.1 Preparation of the Plant Sample

3.1.1 Collection and Proper Identification of the Plant Sample

At first with the help of a comprehensive literature review *Stereospermum chelonoides* was selected for this investigation. The leaves were collected from Jahangirnagar University, Dhaka, Bangladesh during the month of June. The plant is identified by Mr. Rahim and a specimen of this is submitted for further investigation. The Accession no. was DACB43467.

3.1.2 Plant Material Preparation

The leaves of the plants were collected in fresh condition. It was sun-dried to make suitable for grinding purpose. The coarse powders were then stored in air-tight container with necessary markings for identification and kept in cool, dark and dry place for the investigation. Total amount of the dried powder was approximately 1 kg.

3.1.3 Extraction Procedure

Half of the powdered plant material were submerged into it's three times of methanol and petroleum ether solvent (For example: 400 mg of the dried powder was dissolved in 1200 L of the particular solvent) in an air-tight flat bottomed container for seven days, with occasional shaking and stirring. The major portion of the extractable compounds of the plant materials were dissolved in the solvent.

3.1.4 Filtration of the Extract

After the extraction process the plant extract was filtered with soft and thin square piece of cloth.

↓

Then filtered with sterilized cotton filter fitted in the funnel.

↓

Then again it was filtered with man's filter paper, used for getting more clear extract.

↓

Then the filtrate was taken into a volumetric flask and covered with aluminum foil paper.

↓

Finally the filtrate was prepared for rotary evaporator

Fig 3.1 Rotary Evaporator

3.1.4.1 Procedure

- After the filtration process two parts were obtained namely ‘residual part’ and filtered part or filtrate‟.
- The filtered part, which contains the substance soluble in methanol and petroleum ether, was putted into a 1000ml round bottom flask and then the flask was place in a rotary evaporator.
- The evaporation was done at 50 degree temperatures for methanol and not more than 20 degree as petroleum ether is volatile.
- The number of rotation per minute was selected as 60 rpm. The pressure of the vacuum pumper machine was 6bar.
- The water flow through the distillation chamber was also provided in a satisfactory flow rate.
- When the evaporation seemed to be satisfactory, then the methanol extract was collected in a 50mL beaker.
- The extraction was collected from the evaporating flask and the solvent is collected from the receiving flask.
- The evaporator flask was rinsed by methanol in case of the extract of methanol and for petroleum ether extract, it eas rinsd with petroleum ether.
- Then the beaker was covered with aluminum foil paper and kept for 60 minutes.
- Finally the concentrated methanol plant extract was found and stored in the laboratory refrigerator from which the extract was used for many chemical investigations.

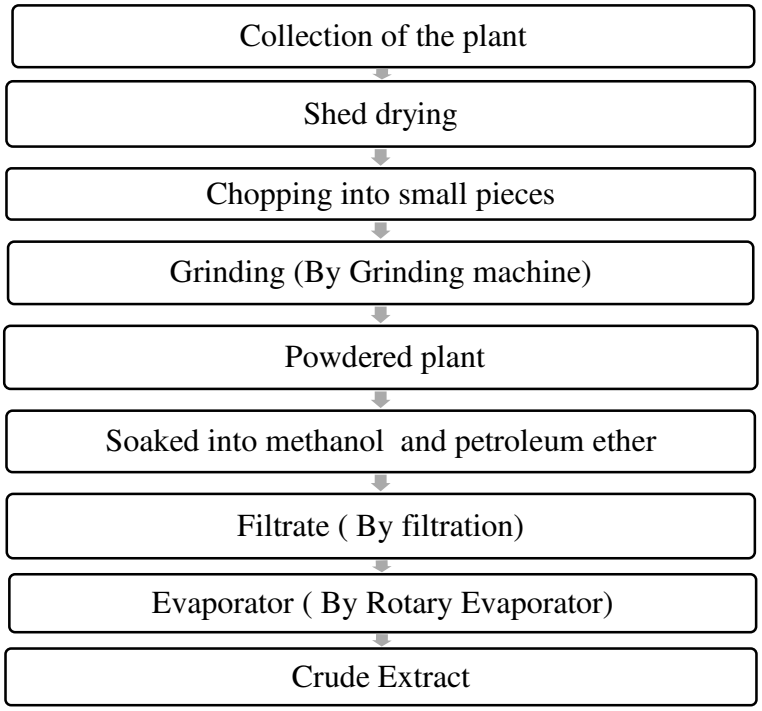


Figure 3.2 Schematic Presentation of the Crude Preparation From The Plant

3.2 Tests For analgesic activity

3.2.1 Principle

In this method acetic acid is administered intra-peritoneal to the experimental animals to create pain sensation. As a result, the animals squirms their body at regular interval out of pain. This squirm/contraction of the body is termed as “writhing”. As long as the animals feel pain, they continue to give writhing. Each writhing is counted and taken as an indication of pain sensation. Any substance that has got analgesic activity is supposed to lessen the number of writhing of animals within in a given time frame and with respect to the control group. The writhing inhibition of positive control was taken as standard and compared with test samples and control. As positive control, any standard NSAID drug can be used.

3.2.2 Drugs:

Indomethacin were used for current study which was supplied from Novartis Pharmaceuticals Ltd, Bangladesh

3.2.3 Experimental Animal

Swiss-albino mice of either sex, aged 4-5 weeks, brought from the Animal Resource Branch of the International Centre for Diarrhoeal Diseases and Research, Bangladesh (ICDDR, B) were used for the experiment. The average weights of the mice were 24 to 38 gm. Standard environmental situation was maintained to keep the mice. The condition was 55-65% relative humidity, 12 hours light/dark cycle and 24.0±0°C temperature. Also sufficient amount of food and water was supplied all the time.

Figure 3.3 Swiss Albino Mice in Cage

Animal feed: 'Mouse-pellets' supplied by ICDDR, B Dhaka.

Material used for animal housing: Plastic cages having a dimension of (28×22×13) cm; Soft wood Shaving.

Fig 3.4 Swiss Albino mice Ready for Dosing

3.2.4 Identification of animals during experiment

forty experimental mice were randomly selected and divided into ten groups containing four mice. Each group received a particular treatment i.e. control, standard and two different doses of the extract of methanol and petroleum ether extract. Prior to any treatment, each mouse was weighed properly and the doses of the test samples and control materials were adjusted accordingly. It is difficult to identify and observe at a time five mice receiving same treatment. Thus it was important to identifyindividual animal of a group during the treatment. To denote individual animal, they were marked or coded I, II, III, IIII.

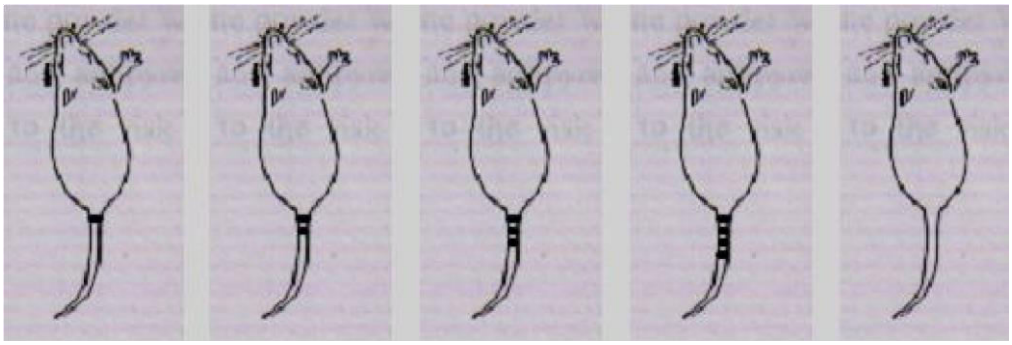


Fig 3.5 . Marks used for identifying experimental mice

3.3 Pharmacological investigation of plant extracts

Analgesic activity tests were done as pharmacological investigations to determine the medicinal effect of the experimented extracts:

3.3.1 Analgesic activity of *Stereospermum chelonoides* plant extracts

Drug which is used to relieve pain is called analgesic drug. These drugs are also known as painkiller. The analgesic test was done by the method:

Acetic acid induced writhing technique

3.3.2 Design of the analgesic experiments

Thirtysix mice were chosen anyway and divided into six groups where the groups were from G1 to G6 as well as 6 mice were in each group. Each group got a specific treatment. Before the treatment, each mouse were weighed properly as well as marked. Then the dosage of the test sample and control materials was also settled according to body weight. Carboxy Methyl Cellulose was used to make the extract soluble while making the dose.

Group-G1- water

Group-G2- Standard (Indomethacin)

Group-G3- SCLM 250 mg/kg

Group-G4- SCLM 500 mg/kg

Group-G5- SCLPE 250 mg/kg

Group-G6- SCLPE 500 mg/kg

Figure 3.6 Oral Dose Administration

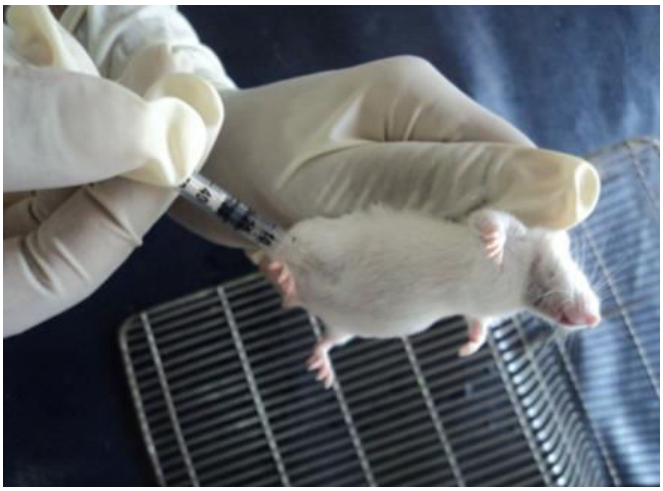


Figure 3.7 Peritoneal Acetic Acid Administration

Figure 3.8 Writhing Test

3.3.3 Acetic acid-induced writhing technique

Acetic acid induced writhing test is a technique where analgesic behaviour is observed (Ahmed *et al*., 2001). In this method, intra-peritoneally acetic acid was administered to the mice so that pain sensation generates. Here, indomethacin was considered as standard. Six groups of 6 mice each were pretreated with the methanolic extract (250 mg/kg, 500 mg/kg P.O, Body Weight), petroleum ether extract (250 mg/kg, 500 mg/kg P.O.Body Weight), control and standard orally. After 30 minutes, the solution of 0.7% v/v acetic acid was administered intra-peritoneally. After administration of solution of acetic acid, no writhing was counted for 5 minutes. After 5 minutes, writhing was counted for 15minutes. For that each mouse was placed on observation table and noticed the number of writhing of mice. The mice did not give full writhing all the time. They gave half writhing also. So, two incomplete writhing were counted as one complete writhing.

The percentage inhibition was calculated using the formula:

$$\% \text{ Inhibition} = \frac{\text{Mean no. of writhing (control) - Mean no. of writhing (drugs)}}{\text{Mean no. of writhing (control)}}$$

3.3.4 Statistical analysis

Total values which were obtained from the experiments are represented as mean ± standard error of the mean (SEM). Statistically obtained data was estimated by using ANOVA (Analysis of variance) followed by post-hoc Dunnett's test which was associated with SPSS program (SPSS 17.0, USA). The results obtained were compared with the vehicle control group. p values < 0.05, 0.01 and 0.001 were considered to be statistically significant.

CHAPTER: 4

RESULT & DISCUSSION

4.1 Results of Acetic acid induced writhing test (peripheral pain)

In this test, analgesic effects of plant *Stereospermum chelonoides* were investigated by administering 250 mg/kg and 500 mg/kg dose. By applying this test, it was seen that SCLM produces significant analgesic effect ($p<0.05$) at the dose of 500 mg/kg in a dose depending manner whereas SCLPE also seemed to inhibit pain. The inhibition of SCLM, SCLPE at the doses of 250 mg/kg and 500 mg/kg were 8.36%, 51.51%, 10.03% and 31.44% respectively. It was seen that the inhibition was increased at the dose 500 mg/kg compare to the 250 mg/kg dose. For the standard (Indomethacin) the inhibition was 86.96%. However, all the results were statistically significant.

Table 4.1– Result of Analgesic activity test of SCLM by acetic acid induced writhing method

Group	Treatment	Dose	No of writhing (Average ± S.E.M)	Percent Of Inhibition
Group-1 (Control)	**Water**	**10mL/kg**	**49.83±12.48**	**----**
Group-2 (Standard)	**Indomethacin**	**10mg/kg**	**6.50±4.59*** **	**86.96**
Group-3 (Extract)	**SCLM**	**250mg/kg**	**45.67±9.20**	**8.36**
Group-4 (Extract)	**SCLM**	**500mg/kg**	**24.17±13.23***	**51.51**

Each value is presented as the mean ± SEM (n = 6). *p < 0.05, **p < 0.01, ***p < 0.001, (n=6) Dunnett's test compared with control group.

Table 4.2– Result of Analgesic activity test of SCLPE by acetic acid induced writhing method

Group	Treatment	Dose	No of writhing (Average ± S.E.M)	Percent Of Inhibition
Group-1 (Control)	**Water**	**10mL/kg**	**49.83±12.48**	**----**
Group-2 (Standard)	**Indomethacin**	**10mg/kg**	**6.50±4.59*****	**86.96**
Group-3 (extract)	**SCLPE**	**250mg/kg**	**44.83±12.32**	**10.03**
Group-4 (extract)	**SCLPE**	**500mg/kg**	**34.17±23.36**	**31.44**

Each value is presented as the mean ± SEM (n = 6). *p < 0.05, **p < 0.01, ***p < 0.001, (n=6) Dunnett's test compared with control group.

Here,

SCLM= *Stereospermum chelonoides,* Leaves, Methanol

SCLPE= *Stereospermum chelonoides,* Leaves, Pet Ether

4.2 Discussion:

Narcotics or non-narcotics (NSAIDs) drugs are employed for the pain management. For the production of commercial drugs or in the improvement of lead compounds, it has been built that medicinal plants are good reservoir of it. However these drugs have toxic effects also (Park *et al*., 2004). From the analgesic activity results and the reduction in the number of writhes compared to the control groups was considered as evidence of analgesic effect in *Stereospermum chelonoides*.

Pain is an unpleasant and emotional experience associated with tissue damage. Analgesics are the drugs used to relieve pain. Inflammation causes trigger in inflammatory mediators such as TNF-α, interleukins and prostaglandins. Anti-inflammatory agents are capable of inhibiting the cyclooxygenase COX-1 and COX-2 pathway of arachidonic acid metabolism, which produces prostaglandins thus reduce the pain sensation (Tasleem *et al*., 2014). Classical analgesics of natural origin include opiates and non-steroidal anti-inflammatory drugs but they are associated with side effects such as gastric lesions and tolerance and dependence (Ezeja *et al*., 2011). So, there is a need to explore natural available alternative sources to NSAIDs and opiates.

Acetic acid-induced writhing test is the most commonly used test to assess peripherally acting analgesics. Writhings generated by parenteral administration of acetic acid in mice, are due to profound pain of endogenous nature which recur for a prolonged period of time. Writhing is an explicit response to the intense pain induced by irritant principles via nociceptors characterized by episodes of retraction of abdomen and stretching of hind limbs. The signals transmitted to central nervous system in response to pain due to irritation, cause release of mediators such as prostaglandins which contributes to the increased sensitivity to nociceptors (Shivaji P.G., 2012).The increase in prostaglandin production further enhances the vascular permeability. The decrease in the number of writhings assumes decrease of prostaglandins synthesis which results in significant analgesic activity. Acetic acid induced abdominal constriction is a standard, simple, and sensitive test for measuring analgesia induced by both opioids and peripherally acting analgesics. This test,

besides being the most appropriate anti nociceptive model for opioids, is also commonly employed as a visceral inflammatory pain model (Hayes *et al*., 1987).

Table 4.1 and 4.2 show that extracts reduced the number of writhing movements induced by the i.p. administration of acetic acid solution. The methanolic extract shows significant result in ANOVA test (p value < 0.5) and the standard is highest significant comparing all other groups.

These data also suggest that the extract can produce analgesic action through inhibition of COX (Inhibition of the enzyme cyclo-oxygenase) and consequently prostaglandin synthesis. But this inhibition of pain may also occur due to phytochemical constituents which is present in the extract of the experimented plant. Phytochemical screening of SCL gives evidence of containing some secondary metabolites, such as polyphenols, flavonoids, alkaloids, terpenoids and glycosides which have gained importance due to their diverse pharmacological activities such as anti-inflammatory, analgesic and antipyretic, etc. (Mohammad *et al*.,2006)

Significant analgesic activity was shown by plants that contain organic acids and flavonoids (Sasikala *et al*., 2011). Flavonoids may attribute to a number of pharmacological activities. Some flavonoids are reported to possess significant analgesic and anti-inflammatory activity. Some flavonoids can significantly interfere with inflammatory mediators (Ullah et al., 2014). Certain members of flavonoids significantly affect the function of the immune system and inflammatory cells. A number of flavonoids such as hesperidin, apigenin, luteolin, and quercetin are reported to possess anti-inflammatory and analgesic effects. Flavonoids may affect specifically the function of enzyme systems critically involved in the generation of inflammatory processes, especially tyrosine and serine-threonine protein kinases. The inhibition of kinases is due to the competitive binding of flavonoids with ATP at catalytic sites on the enzymes. These enzymes are involved in signal transduction and cell activation processes involving cells of the immune system. It has been reported that flavonoids are able to inhibit expression of isoforms of inducible nitric oxide synthase, cyclooxygenase, and lipooxygenase, which are responsible for the production of a great amount of nitric oxide, prostanoids, leukotrienes, and other mediators of the inflammatory process such as cytokines, chemokines, or adhesion molecules.

Flavonoids also inhibit phosphodiesterases involved in cell activation. Much of the anti-inflammatory effect of flavonoid is on the biosynthesis of protein cytokines that mediate adhesion of circulating leukocytes to sites of injury. Certain flavonoids are potent inhibitors of the production of prostaglandins, a group of powerful proinflammatory signaling molecules (Shashank and Abhay, 2013).

Reversal of the carrageenan induced inflammatory changes has been observed with silymarin treatment. It has been found that quercetin inhibit mitogen stimulated immunoglobulin secretion of IgG, IgM, and IgA isotypes in vitro. Several flavonoids are reported to inhibit platelet adhesion, aggregation, and secretion significantly at 1–10 mM concentration .The effect of flavonoid on platelets has been related to the inhibition of arachidonic acid metabolism by carbon monoxide. Alternatively, certain flavonoids are potent inhibitors of cyclic AMP phosphodiesterase, and this may in part explain their ability to inhibit platelet function (Shashank and Abhay, 2013).

CHAPTER: 5

CONCLUSION

5 Conclusion

Drugs used for analgesic and anti-inflammatory activity (Narcotics and NSAIDs) can produce significant adverse effects so more and more production of these types of drugs from natural sources with limited adverse effect is widely needed. Among all the natural sources surrounding *us Stereospermum chelonoides* is also a nature's gift to us which contains pharmacological activity to give analgesic activity. From the acetic acid induced analgesic test we have found that, the SCLM and SCLPE increase the inhibition percentage at the dose 500 mg/kg compared to 250 mg/kg.. After observing the results of recent study, it can be said that SCLM extracts of our experimental plant leaves at dose of 500 mg/kg showed significant ($p<0.05$) analgesic activity wheras SCLPE gives good analgesic effect with the increased dose. These indicated that this plant could be a potential source for discovery of newer analgesic and anti-inflammatory "leads" for drug development.

So it is clear that our experimental plant on which we have worked is helpful plant but our work was only preliminary effort which will require further comprehensive exploration as well as depiction of active compounds to elucidate the mechanism of action of producing the analgesic effects of the extract and necessitates preformulation studies for expansion of a potential dosage form.

Chapter 6

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