Literature Review

Different parts of *Lantana Camera* Linn are used for the treatment of various human ailments. It is one of the most prevalent and weeds causing hepatotoxicity. Literature emphasized on different bioactive molecules present in the Lantana camera Linn. Present survey focused on bioactive molecule Lantadene and therapeutic uses.

WOUND HEALING ACTIVITY

Wound healing is the body’s natural process of regenerating dermal and epidermal tissue. Collagen accounts for 30% of the total protein in the human body. In normal tissue Collagen provides strength, integrity and structure. When tissues are disrupted following injury, collagen is required to repair and restore normal structure and function (Prockop D. et al; 1995) However thermal burns to the skins produce a remarkably different healing response due to their effects on the cells and tissue. Beyond the area of total destruction induces nutrient starvation of involved tissue. Apart from thermal injury wound may arise due to physical injury and chemical injury or microbial infections. *Lantana Camera* used as herbal medicine for the treatment of antiseptic for wounds (Saxena V. et at; 1999).

The Ethanol extract of it, increased the rate of wound contraction by 87% in burn wound when compared to control 82%. The slight reduction in wound area might due to antimicrobial effect of the leaf extract. Data demonstrates that the *Lantana Camera* Linn has antimicrobial activity but not wound healing activity on burn wound in rats. (Nayak B.et al;2008) while it found reverse in number of plants that find use as wound healing during the course of the survey. The information has been counterchecked with that available in other places (Patil S.et al; 2009)

ANTI MOTILITY ACTIVITY

Diarrhea is one of the most prevalent human disorders. Antimotility compounds such as dipheoxylate, loperamide, opium alkaloids, anticholinergics etc have been tried against diarrheal disorders but often with side effects after prolonged use (Hoonson D. et al;2001). Evaluation of anti motility activity was done in intestine of mice treated with *Lantana camera* L. Leaf powder, neostigmine used as a promotility agent. Intestinal motility was assessed by charcoal meal test. The anti diarrheal effect of lantana leaf extract was studied against castor oil induced diarrhea model in mice. The percent intestinal transits was increased significantly with neostigmine but it
was decreased significantly by all concentration of *Lantana camera* methanolic extract and Lantadene A. *lantana camara* methanolic extract (LCME ) dose of 1000 mg / kg intestinal transits was nearly abolished. (Sagar L.et al; 2005)

**ANTI ULCEROGENIC ACTIVITY**

Methanolic extract of *Lantana camera* L. has been reported anti ulcerogenic activity. Oral administrations of methanol extract of *lantana camera* L. exhibited dose dependent inhibition. Methanolic extract of *Lantana Camera* Linn leaves was evaluate gastric ulcerogene is in Pyloric ligated rats, ethanol induced gastric ulcers and duodenal ulcer model. It also has healing of gastric ulcer and also prevents the development of duodenal ulcer in rates (Sathish R. et al; 2011)

**ANTI MICRO – BACTERIAL ACTIVITY**

*Pseudomonas aeruginosa* is an infection that usually affects hospitalized or immuno compromised person. Usually occurs infection of the airways by *Pseudomonas. aeruginosa* occurs commonly in patients with cystic Fibrosis but occurs in patients with other forms of bronchiectasis (Miszkie K. et al; 1997) In view of high antibiotic resistance the infections associated to *Pseudomonas. aeruginosa* are considered to have difficult management.

The results of antibacterial tests by gaseous contract showed that; antibiotic activity of amikacin against *Staphylococcus aureus* was enhanced in the presence of the essential oil by gaseous contact.

Enhancement of antibacterial activity of amikacin and gentamicin against *Pseudomonas* aeruginosa by the essential oil was verified too. The improvement of antibacterial activity against the gram negative bacteria showed a significant result as the gram positive bacteria are more susceptible to natural products. Many plants have shown not only antibacterial properties but also the ability to interfere with the antibiotic resistance. (Sousa E.et al; 2011). The study can justify the popular use of L. camera to treat respiratory infection.( Sousa E.et al; 2012)

In another investigation the essential oils of *lantana camera, L,Ocimum sanctum* and *Tagetes patula* were effective against all the bacterial strains when grown in nutrient agar. Essential Oil of Targets Patella leaves completely inhibited the growth of *Escherichia Coli*. Even at lower concentration of Lantana camara Oil was unable to inhibit *Escherichia. Coli* growth.(Dharmagadda V. et al ;2005.)
Bacterial strains included Gram positive *Staphylococcus aureus* and *staphylococcus saprophiticus*, Gram negative *Escherichia coli* and *pseudomonas aeruginosa*; antibacterial activity was determined by disc diffusion method. After the incubation period the inhibition zone was around the discs were measured. Results showed that petroleum ether root extract shown less antibacterial activity on *Pseudomonas aeruginosa* and *Staphylococcus saprophiticus*. The inhibitory zone size of gram positive bacteria indicates less sensitive to the root extract of *Lantana camera* L. The maximum inhibitory zone was reported against *Escherichia coli* in methanol stem extract as compared to the other extract. Saponin and tannins are reported to possess antibacterial activities. Flavonoids and alkaloids isolated from plant are commonly found to have antibacterial properties. (Kensa M., 2011) Variety of chloroform extract of the leaf, stem and root has highest inhibition effect against *Escherichia coli* (Viji M. et al.; 2011) (Pattnaik S.et al; 2010)

Presence of flavonoids along with other natural products has been reported from different medicinal plant extracts. For example *Aloe Vera* used against bacteria; it may also help in strengthening the immune system. Basil, tulsi leaves was studied for antiviral and antibacterial and other medicinal activities. (Sharma D. et al ;2006 )

The literature has shown that gram positive bacteria are more sensitive to antibiotics while gram negative bacteria display some particularities that inhibit censibiotic penetration. Researcher suggest that data obtained may suffer seasonal influence and associated with the presence of Chemical compounds from lantana species.

Antibacterial activities of *L. camera* leaves and flowers were analyzed that flower extracts possess strong antibacterial activities more than the corresponding leaf extracts. Analysis revealed that highest bacterial inhibitory effects against *Basilus substillis* by *L. camera*. Yellow flower ethyl acetate extracts was found to be the most effective against all the bacteria except *Staphylococcus. aureus*. The yellow, lavender, red and white flower of Lantana. camera plants displayed variable antibacterial activities. (Ganjewala D.et al; 2009)

The general photochemical groups of compounds in the aqueous extract were identified by preliminary photochemical screening. Catchin is reported in petroleum ether and methanol extracts.
ALLELOPATHIC ACTIVITY:

There are allelochemicals present in all the parts of shrub. When these chemicals released in surrounding, interferes with germination of many species. Its leaf, stem and root contain some harmful allelochemicals that inhibited the germination and growth of Bryophytes. The inhibition of regeneration process in different ESE plant of *Pogonatum aloides* was found in the decreasing order of apical, basal and middle explants. Basal part show higher regeneration as compared to control and middle explants. (Choyal R. et al ;2011).

ANTHELMENTIC ACTIVITY:

Helminthes infections are among the most common infections in man, affecting proportion of population all over the world. Helminthes still cause considerable problem for human beings and animals. Successive leaf extracts of *lantana camera* showed significant anthelminic activity on selected worms. Anthelmintic activity was assessed using healthy adult Indian earthworms *Pheratima Postuma* due to its anatomical and Physiological resemblance with the intestinal round worm parasites used in assessment of Anthelmintic activity. Ethanolic extract found to more active compared to other solvent extracts. Methanol extracts from the leaves, stems and roots of lantana camera were investigated for their anthelmintic activity against Pheritima Posthuma. (Patel J. et. al; 2011.)

ANTI CANCER ACTIVITY:

Several triterpenoids naphthaquinones, flavonoids alkaloids and glycoside isolated from *lantana camera* L. are known to exert diverse biological activities including anticancer properties. Investigation on the in vitro cytotoxic properties of crude extract of different pasts of *Lantana camera* was taken up against 4 cancerous cell lines and normal cell line using standard procedure. Of the five methanol extracts obtained from different parts of *L camera* L. the leaf extract exhibited comparatively more cytotoxic activity against all the cell lines tested. (Raghu C.et al;2004) Flavonoids and flavonolignans may offer a great scope for the drug development in future such as breast cancer. (Sharma D. et al; 2006)
ANTI FUNGAL ACTIVITY:

Since fungicides are very expensive and cause serious environmental pollution control strategies are today directed towards replacing the use of hazardous chemical fungicides by environmentally friendly natural products.

The antifungal activity of the extracted essential oil derived from the flowers of *lantana camera* towards the three pathogenic fungi was studied in vitro. It also have the potential of becoming powerful and safe alternative means of disease control instead of the harmful pesticides. (Eweis M.et al; 2011), (Goswam-Giri A.et al; 2011)

According to revelations, antifungal compounds present in the plants are active at different stages of germination growth. The isolated basic proteins from Lantana especially the high molecular weight tractions of protein showed the novel antifungal properties which can be used in crop improvement program of sugarcane. (Hiremath L.et al; 2011)

CYTOTOXICITY:

*Lantana camera* L. is one of the most prevalent and noxious weeds causing hepatotoxicity in grazing animals. Recently the cell culture method was used for the production of secondary metabolites of L. Camera cells in suspension cultures and reported to possessed cytotoxic activity. In addition other researchers used the aqueous extracts (0.23%) obtained from L. camera (50 gm dry mass) showing it had an apparent cytotoxic effect of He La Cells with LC$_{50}$ value of 1500 microgram / ml in 36 h. Cytotoxicity test on Vero cell line showed that leap extract concentration up to 500 micro gram / ml inhibit the growth of cell cytotoxicity started to decline at elevated concentration. Authors suggested that acute oral toxicity of the leaf extract should be very useful for clinical study. (Pour B et al ;2011.)

Brine Shrimp lethality test (BST) was used to predict the cytotoxic activity in the plant extract. The lethality of the methanolic of leaf, shoot and root variety to brine shrine was determined after 24 hours of exposure. The % mortally increased with increased with increased with increase in concentration of extracts of leaves, shoots and root. From the study it can be concluded that the leaves of Ashwagandha and roots are effective in cytotoxic activities (Vjji M. et al; 2011). Brine Shrimp Artemia Salina also known as sea monkey is a marine invertebrate about 1mm in size, are used for determination of bioactivity of the L. camera extract. Bioactivity
measured by the brine shrimp lethality test which tests evaluates different pharmacological activities of natural remedies. Some other toxicological researchers using brine shrimp bioassay confirm that the lethality of L. camera extract of various parts are considerably lower than studied plant. Brine lethality test is useful to detect antitumoral compound in terrestrial plant extract (Pour B. et al; 2011).

In the history, clinical signs, diagnostic findings, necropsy findings and exposure to the toxic plant *Lantana camera* support the diagnosis of secondary photo-sensitilization and hepatotoxicity in a Red kangaroo (Harvey J.et al;1998).

**NEMATICIDAL ACTIVITY**

Root knot nematode is one of the most harmful nematode pests in both tropical and subtropical crop production regions and cause extensive economic damage, (Sikora R. et al; 2005 ). The nematicidal and nematostatic activities of L. camera against root nematodes have been is vitro and in soil. It was investigated that L. camera acquires leaf extract did not act as strong nematicide on the juveniles were not killed but only paralyses and consider as nematosetic effect. (Ahmad F.et al; 2010)

**INSECTICIDAL ACTIVITY**

Food security in sub Saharan Africa largely depends upon improved food productivity through the use of GAPS. Some synthetic insecticides penetrate into stored grains and may be toxic (Lalah J. et al; 1996). *Lantana camera* L. have shown to have toxic and repellent effect against certain insect pests of stored grains. The results of percent insect damage during 150 days of storage of untreated grains and those treated with different rates. The untreated grains suffered significant percent damage on stored maize grains. Pesticides in make storage significantly reduce grain damage with no adverse effects on send germination. (Ogendo J. et al; 2004 )

In another investigation, Maize treated with *lantana camera* and *Tepherosia Vogelii* was significantly repellent against *Sitophiloe zamias*. The insect mortality and repellency study suggested that there exists good potential for the two local plant species and can be effectively used as grain proficient in the traditional resource- poor farming. (Ogendo J. O. et al; 2003 )
Experimental study showed that, spraying 10% *lantana camera* leaf water extract once a week in the field did not control *Oulema pectoralis* pest infestation but enhanced the number of leaf, flower, stalk, bud and bloom in Mokara charak pink orchid. Orchid plant growth was not affected by the frequency of extract spraying even though vegetative leaf number or production was enhanced (Binti N. et al; 2010)

**ANALGESIC, ANTI-INFLAMMATORY AND ANTI HEMORRHOIDIAL ACTIVITY:**

First time demonstration of the analgesics, anti-inflammatory and anti-hemorrhoid activity of *Lantana camera* exhibited the anti-inflammatory activity on rats, indicating that the acquires extract of *lantana camera* 300 mg / kg exhibited mild decrease in paw volume but when treated with 500 mg / kg showed significant decrease. Anti-hemorrhoid activity showed significant reduction in signs and symptom of acute hemorrhoidal attack at last week. No significant adverse effects were reported (Gidwani B. et al; 2009).

**ANTIPYRATIC ACTIVITY:**

The antipyretic activity of *Lantana camera* could be at least in part due to enzyme inhibition and free radical scavenging activities which may be attributed the presence of flavonoids and other polyphenols in the extract (Bharagava S. et al; 2008). This study was provided a scientific support for the use of *Lantana camera* for the treatment of pyrexia. (Jain S. et al; 2010)

**LARVICIDAL ACTIVITY:**

Mosquito borne diseases are one of the world’s most health hazardous problems. Several mosquito species belonging to genera *Anopheles culex* and *Aedes* are the pathogens of various diseases. Therefore, need to prevent mosquito borne disease by killing mosquito at larval stage. Synthetic insecticide resistance, pollution, toxic side effects on human beings (Zang L. et al; 2005) Extracts from leaves, flowers and roots of plants and oils were found to have mosquito larvicidal activity. The GC / MS analysis of compounds in methanol flowers and leaf extract of *lantana camera* found to have larvicidal activity, mosquito control agent. (Sathish M. et al; 2008). *Lantana camera* acts as adulticidal activity against different mosquitoes. Adulticidal activity of the oil was highest against *An. Flaviatilis* followed by *An. Culicifacies*. Due to low volatile nature of oil impregnated paper revealed that it possessed more adulticidal activity for
longer period some of the major components of essential of L. camera identified insecticidal properties. (Due K. el al; 2010)

**BIO CHEMICAL COMPOSITION:**

The Phytochemical studies on the stem from the red, pink and yellow flowering taxa of lantana camera reported 13 compounds from the leaves of yellow flowering taxa of this plant. They were isolated from the ethylacetate and identified by Spectroscopic method and GC analysis (Sharma O. et al ;1998).

Eight triterpenoids, betulonic acid (3), Betulinic acid, O leanolic acid, Lantadene A, Lantadene B, Icterogenin, lantanilic acid, ursolic acid, three flavonoids, hispidulin, Pectolinarinigenin, Pectolinarin as well as β-sistosteryl 3– 0- β D glucoside and a mixture of campestral, Stigmasteoool and β- Sitesterol were isolated from the leave of the yellow flowering taxa of *lantana camera* (Juang F.et al; 2005 ) The stems from the red flowering taxa, yellow flower and pink flowering taxa of *Lantana camera* Linn compounds were investigated and isolated by using ethyl acetate fraction. It was chromatographed on a silica gel column using a mixture of Chloroform- Methanol with increasing solvent polarity as elutant to give 3 fractions. Fraction I was purified by repeated column chromatography on silica gel eluted with n-hexane ethyl acetate to afford phytosterols, 3-β-hydroxystigmaol-5-en-7 one oleanolic acid, betulonic acid, betulinic acid and oleanolic acid. Fraction II was further Chromatographed on a Silica Gel Column with n-Hexane by increasing concentration of acetone to yield lantadene A, lantadene B, 22-B-angeloyloxyantanolic acid and lantanilic acid. Fraction III was rechromatographed on a Silica gel column with Chloroform and methanol as eluent to give pomolic acid and β- sitosterd-3-0- β-D glucoside (Huan K et.al ;2004)

*Lantana camera* leaves was found to be highly toxic, Red Flowers, Yellow Flowers showed against adult beetles (*Mylabris Phalerata Pallas* ). Least mortality response around zero was obtained in case of Yellow flower,( Sharma T.et al; 2011) for this purpose 15 species of plant were used. By means of bio guided, purification procedure more than 30 novel compounds were isolated, purified and characterized. Among the identified compounds showed therapeutic medicinal properties ( Nogueiras C.et al ;2010)

Extraction of *lantana camera* in various polar and non polar solvents resulted in high amount of extractives in hot water than those obtained in organic solvent. Petroleum ether a non
polar solvent isolated a very low amount of extractives. There are more extractives in aerial parts than those found in root extract (Chandra A. et al; 2010).

Day time, the plants active substances constituent concentration is less or higher and Temperature, relative humidity, sun exposition are fundamental factors that are able cause variation. Result showed that there was significantly difference between the essential oil yields obtained from different collect time. The less yield 0.01% was recorded at 7.00a.m. and the higher one 0.09% was obtained at 7.00 pm. (Barreto F. et al; 2010)

During investigation, determined Chemical Components from Lantana Camera Leaves by GC- MS method,18 compound were identified (Jancyranil P. et al; 2011).

For performing qualitative phytochemical analysis the fruit of Lantana camera Linn were studied and analysed by TLC and HPTLC which shows a set of diagnostic characters (Vekatachalaram T. et al; 2011)

**LANTADENE AND ITS BIOACTIVITY:**

*Lantana camera* L. provides a huge amount of biomass that is interest to exploit for natural product in drug research. Some pentacyclic tri-terpenoids are known to have anti-inflammatory. (Sharma O. et al; 2000)( Sharma O. et al ;1992) antitumor or anti-AIDS activity lantadene isolated from L. Camera belong to the oleanane series which have attracted considerable interest mainly because of their toxicity and antitumor activity (Sharma M. et al; 2011)

Lantana leaf extracts exhibits tumor inhibitory activity in a two stage carcinogenesis model in nice. It was also found that compound induces apoptosis in human leukemia HL- 60 cells (Reed J. et al; 2001). These compounds differ in the structure of the group attached C- 22 and there are indication that the structural variations involving C-22, C-17 in the antitumor activity of Lantadene A. The cytotoxicity profile at different derivatives showed that with removal of the ester at C-22.There was significant decrease in the activity whereas methylation of C-17 carboxyl group resulted in some activity. An increase in the activity and branching decreased the activity. An aromatic ester at C-22 also resulted in decreased activity. These results indicate the importance of the C-22 and C-17 position in the antitumor activity (Sharma M. et al 2008 ) The results interference the importance of the group attached to C-22 and C-17 in relation to the antitumor activity of Lantadene molecule.
A tumor is a disease state characterized by uncontrolled proliferation and absence of apoptosis. During apoptosis, the cell experiences a cascade of events that ultimately result in nuclear condensation and DNA fragmentation. Thus induction of apoptosis is an efficient method of treating cancer. Lantadene A is the most abundant in the *Lantana camera* var. aculeate (Red). However the molecular mechanism responsible for its tumor activity inhibitory potential is not well understood. For isolation of lantadene the partially purified Lantadene fraction was chromatographed over a silica gel column using chloroform and chloroform-methanol as the eluting solvent. The solvent was removed in vacuum and the resulting solid residue was recrystallized twice from methanol to obtain pure Lantadene A as white crystals M.P. 283°C. Effect of Lantadene A on the proliferation of HL-60 cancer cells was determined by using the MTT assay. Lantadene A significantly inhibits cell proliferation of HL-60 cancer cells and induces well apoptosis (Sharma M. et al; 2007)

Considering Chemotherapeutic uses of Lantadene A, vibrational spectra of the important biological molecule Lantadene A were studied yet, no detailed quantum chemical calculation has been performed on Lantadene A. Isolation of Lantadene A and its recrystallisation give white crystalline Lantadene A (M.P.280-82°C) The frequency assignments for Lantadene A have been done for FTIR Spectra. It revealed comparable results and lower computational time; semi empirical method could be used to study the spectra of lantadene A. (Dwivedi A. et al; 2009.)

Injection of Lantana foliage causes cholestasis and hepatotoxicity in animals. Lantadene A and C are hepatotoxic to guinea pigs while Lantadene B an isomer of Lantadene A has been found to be nontoxic (Nethaji M. et al; 1993).

Literature survey is intensely fruitful for the present investigation. It will give guidelines for collecting data, selecting proper methodology, appropriate statistical analysis, selecting parameters and new working methodology such as Nanotechnology. Nanotechnology approach will help researcher new direction to molecular recognition (Fertina p.et al; 2000).