3.1 Literature review about of Pain and Inflammation:

Now, and not to get too complicated, but the peripheral mechanism of pain, you have your soft tissue injury. Here you've got stimulation of the COX-2 pathway, and you've got production of prostaglandin-E, which, not to go through too much detail, but the end result is that you have--you decrease the threshold for your neuron firing, so you're sending a lot of signals up to the brain that something's hurting. Now we also know that there are central mechanisms of this pain too.

![Peripheral Mechanisms of Pain](image)

**Fig. 3.1 Peripheral Mechanisms of Pain**
I'm going to get a trigger thumb pushing on this thing. Anyways, the same basic system is occurring here, where you get induction of the COX-2 pathways centrally and you also get production of the prostaglandin, which stimulates the dorsal horn, so it makes it more prone to be fired off, so you get the sort of central sensitization of the pain, which you think would be the worst of all worlds.

Fig. 3.2 Central Modulation of Pain

Now one thing, not to get into too much detail here, but we've been concentrating on your lipid mediators. These are your prostaglandins, but I think we're becoming more and more aware of the fact that this kinin system is actually quite important. You can see all these different kinins here, but these are the ones that are probably important. Your tumor necrosis factor, and your IL1 and the IL6 pathways for the interleukin-1 and the interleukin-6 pathways. You know, these are very, very important in this acute phase reaction--if you want to call it that--in the production of pain.
Fig. 3.3 Mediators of Inflammation

- Lipid mediators
- Kinin forming system
- Cytokines mediating inflammatory and effector functions
- Histamine and serotonin
- Products of the complement system
- Coagulation mechanism
- Fibrinolysis
- Chemotactic factors
- Acute phase reactants
And to give you an example of how important this is, we've had studies where, if you look at what's the best predictor, how well someone's going to do postoperatively, it's not anything to do with central pain, it doesn't really have a lot to do with bleeding and other problems. It really has to do with how much inflammation they're having, and this was a very nice study where they found that the best predictor of how well people were going to do postoperatively is what their interleukin-6 levels were. This is an acute phase reaction, so in other words, the more inflammation they have, the worse they're going to do. And what they found is on the first day postop, that was the best predictor of how long it took them to walk either 10 or 25 m, and by the time of discharge--by the second day--the C-reactive protein level, again another acute phase reaction, was the best predictor of how soon they were going to get out of the hospital and how, you know, good a pain control they were going to have. Nothing central. This is all peripheral.

Fig. 3.4 Interleukin 6 and the Pain Response
And looking at interleukin-1, next slide, you know that was also shown to be able to induce these inflammatory pathways, and, in fact, your prostaglandin-E levels. We have been concentrating on the COX-2 stuff, but the prostaglandin-E levels were increased by 10-fold after they infused these animals with interleukin-1. And you think, well, what's the big deal about that? Well, we can control these. If the animals were given diclofenac, (this is an older study from '88, and so celecoxib and rofecoxib weren't around) but if they were given diclofenac, they were able to virtually shut down this prostaglandin production because of this, that was caused by this infusion of interleukin-1. So these are all factors in peripheral pain production.

Fig. 3.5 Interleukin 1 and the PGE2

- Interleukin-1 (IL-1) has been shown to induce inflammatory reactions through increased prostaglandin production
- PGE2 levels were found to be enhanced more than 10-fold after the infusion of IL-1
- Both the increased pain reflexes as well as the enhanced PGE2 levels were abolished by addition of a COX inhibitor (diclofenac)
- IL-1 may also play a role in peripheral pain sensations
So this is probably the best working model that we have right now of pain. It's not only peripheral, which we tend to think of, it's also central. And so you get the trauma and inflammation. You get prostaglandin production, but remember this interleukin pathway. And we think that this interleukin-6 may be the pathway for the central sensitization, but the bottom line is, you get both peripheral prostaglandin production [and] central prostaglandin production as a sort of an amplification of the pain, and the end result is that the patient says, "Ouch," and they hurt, and they don't like that.

Fig. 3.6 Role of Prostaglandins in Pain
Fig. 3.7 Pathway of Tissue Injury
## Determining Mechanism of Pain

<table>
<thead>
<tr>
<th>Type of Pain</th>
<th>Somatic Pain</th>
<th>Visceral Pain</th>
<th>Neuropathic Pain</th>
</tr>
</thead>
<tbody>
<tr>
<td>Location</td>
<td>Localized</td>
<td>Generalized</td>
<td>Radiating or specific</td>
</tr>
<tr>
<td>Patient Description</td>
<td>Pinprick, or stabbing, or sharp</td>
<td>Ache, or pressure, or sharp.</td>
<td>Burning, or prickling, or tingling, or electric shock-like, or lancinating</td>
</tr>
<tr>
<td>Mechanism of Pain</td>
<td>A-delta fiber activity Located in the periphery$^1$</td>
<td>C Fiber activity Involved deeper innervation$^1$</td>
<td>Dermatomal$^2$ (peripheral), or non-dermatomal (central)</td>
</tr>
</tbody>
</table>
| Clinical Examples | • Superficial laceration  
• Superficial burns  
• Intramuscular injections, venous access  
• Otitis media  
• Stomatitis  
• Extensive abrasion | • Periosteum, joints, muscles  
• Colic and muscle spasm pain$^*$  
• Sickle cell  
• Appendicitis  
• Kidney stone | • Trigeminal  
• Avulsion neuralgia  
• Post-traumatic neuralgia  
• Peripheral neuropathy (diabetes, HIV)  
• Limb amputation  
• Herpetic neuralgia |
| Most Responsive Treatments | • Acetaminophen  
• Cold packs  
• Corticosteroids  
• Local anesthetic either topically or by infiltration  
• NSAIDs  
• Opioids  
• Tactile stimulation | • Corticosteroids  
• Intraspinal local anesthetic agent  
• NSAIDs  
• Opioid via any route | • Anticonvulsants  
• Corticosteroids  
• Neural blockade  
• NSAIDs  
• Opioids (via any route)  
• Tricyclic antidepressants |

$^1$ Most postoperative patients experience A-delta and C fiber pain and respond best to narcotic of any route and NSAIDs.

$^2$ Segmental distribution follows a dermatome chart. This traces the pathway of sensation to its nerve root. A Dermatome Map is available through the ICSI Knowledge Products list in the "Support for Implementation" section of this guideline.

**Opioid responsiveness:** The following is a visualization of how different types of pain respond to opioids:

![Opioid responsiveness diagram]

$^*$ Colic and muscle spasms may be less responsive to opioids. Respond best to antispasmodics, NSAIDs, benzodiazepines, buprenorphine.

---

**Fig. 3.8 Determining Mechanism of Pain**
3.1.1 Pain Disorders:

Fig. 3.9 Pain effect in Brain

Until recently, pain management has been dominated by traditional therapeutic modalities, including opiates and nonsteroidal anti-inflammatory drugs. Recent innovations in pain management have been led by new treatments such as triptans and COX-II inhibitors. Still, side effects of current drugs may prove unacceptable to some patients, and thus, pain management remains an under-served medical need.

Pain therapeutics represents a multi-billion dollar market. Demographics, physician prescribing patterns and novel products are expected to spur significant growth in the pain market over the next decade. Pain disorders are classified into several categories based upon their cause. Neuropathic pain is a particularly severe pain disorder that results from damage to the central and peripheral nervous systems. Inflammatory pain results from the effects of inflammatory mediators and cellular debris that are released into surrounding tissues as the immune system is activated,
whether appropriately to fight infection, or inappropriately, e.g., as in autoimmune disorders, such as rheumatoid arthritis. Both neuropathic pain and inflammatory pain are types of chronic pain.

\[\text{Fig. 3.10 Pain and Injury Relation}\]

We have identified several ion channel targets including sodium channels, calcium channels and potassium channels, that are expressed in pain pathways in both the central and peripheral nervous systems. For several of these targets, we have identified lead compounds with in vivo efficacy in animal models of pain disorders. For example, in our multi-target sodium channel pain program, Icagen has identified selective compounds which demonstrate efficacy in animal models for neuropathic and inflammatory pain.
In August 2007, we entered into a collaborative research and license agreement with Pfizer for the discovery, development, manufacture and commercialization of compounds and products that modulate three specific sodium ion channels as new potential treatments for pain and related disorders. Under the terms of the agreement, we and Pfizer are combining resources to identify compounds that target these three ion channels in a global research and development collaboration. We and Pfizer have formed a joint research committee to monitor and oversee the collaboration.

The ion channel targets included in the collaboration are important in the generation of electrical signals in nerve fibers that mediate the initiation, transmission and sensation of pain. In preclinical studies, compounds identified by us have demonstrated efficacy in pain models. We have also established a broad portfolio of intellectual property in this area, covering multiple promising compounds targeting sodium channels. Under the terms of the collaboration, we have granted Pfizer a worldwide exclusive license, with the right to grant sublicenses, to our patent rights and know-how with respect to drugs arising from the collaboration. In addition, we have granted Pfizer the first right to enforce our intellectual property rights in order to protect these drugs and have retained a right to enforce our intellectual property rights. Pfizer is responsible for funding all aspects of the collaboration and for worldwide clinical development and commercialization of drugs arising from the collaboration.

3.1.2 Pathophysiology of Pain:

Pain is influenced by many factors. The American Academy of Pediatrics along with the American Pain Society, Task Force on Pain in Infants, Children, and Adolescents emphasizes that, “Pain is an inherently subjective experience and should be assessed and treated as such. Pain has sensory, emotional, cognitive, and behavioral components that are interrelated with environmental, developmental, sociocultural, and contextual factors.” Pain is influenced by age, race, gender and
culture. There are two categories of pain: Acute and chronic. Acute pain is usually associated with an injury or pathologic condition (i.e., sore throat) that generally resolves with the resolution of the inciting cause. Acute pain is mediated through nociceptors that fire in response to chemicals released during tissue damage, including leukotrienes, bradykinins, serotonin, histamine and thromboxanes. Prostaglandins do not directly activate receptors; however, they act as a local mediator that enhances the sensitivity of the free nerve endings and produce pain and edema by their vasodilatory effect. Nociceptors can be found in the skin, periosteum, arterial walls, teeth, joint surfaces, and in the falx and tentorium of the cranial vault. Nociceptors propagate their impulses through the peripheral nerve to their cell body in the dorsal horn of the spinal cord to the spinal cord where Substance P (a neurotransmitter) is released, which then relays the signal to the cortex via higher order neurons and the spinothalamic tract. Pain functions as a biologic alarm system to signify tissue damage and prevent further injury. Additionally pain can be divided into somatic, visceral and neuropathic types. Noting the type of pain will help not only in making the diagnosis, but also in choosing the best therapy.

3.1.3 Pathophysiology of inflammation: -

The process of acute inflammation is initiated by cells already present in all tissues, mainly resident macrophages, dendritic cells, histiocytes, Kupffer cells and mastocytes. These cells present on their surfaces certain receptors named pattern recognition receptors (PRRs), which recognize molecules that are broadly shared by pathogens but distinguishable from host molecules, collectively referred to as pathogen-associated molecular patterns (PAMPs). At the onset of an infection, burn, or other injuries, these cells undergo activation (one of their PRRs recognize a PAMP) and release inflammatory mediators responsible for the clinical signs of inflammation. Vasodilation and its resulting increased blood flow causes the redness (rubor) and increased heat
Increased permeability of the blood vessels results in an exudation (leakage) of plasma proteins and fluid into the tissue (edema), which manifests itself as swelling (tumor). Some of the released mediators such as bradykinin increase the sensitivity to pain (hyperalgesia, dolor). The mediator molecules also alter the blood vessels to permit the migration of leukocytes, mainly neutrophils, outside of the blood vessels (extravasation) into the tissue. The neutrophils migrate along a chemotactic gradient created by the local cells to reach the site of injury. The loss of function (functio laesa) is probably the result of a neurological reflex in response to pain.

**Fig. 3.11** Micrograph showing acute inflammation of the prostate gland with the characteristic neutrophilic infiltrate

In addition to cell-derived mediators, several acellular biochemical cascade systems consisting of preformed plasma proteins act in parallel to initiate and propagate the inflammatory
response. These include the complement system activated by bacteria, and the coagulation and fibrinolysis systems activated by necrosis, e.g. a burn or a trauma. The acute inflammatory response requires constant stimulation to be sustained. Inflammatory mediators have short half lives and are quickly degraded in the tissue. Hence, acute inflammation ceases once the stimulus has been removed.

3.1.4 Systemic inflammation and overeating:

Hyperglycemia induces IL-6 production from endothelial cells and macrophages. Meals high in saturated fat, as well as meals high in calories have been associated with increases in inflammatory markers. While the inflammatory responses are acute and arise in response to overeating, the response may become chronic if the overeating is chronic.

3.1.5 Outcomes of inflammation:

The outcome in a particular circumstance will be determined by the tissue in which the injury has occurred and the injurious agent that is causing it. Here are the possible outcomes to inflammation:

1. **Resolution:**
   The complete restoration of the inflamed tissue back to a normal status. Inflammatory measures such as vasodilation, chemical production, and leukocyte infiltration cease, and damaged parenchymal cells regenerate. In situations where limited or short lived inflammation has occurred this is usually the outcome.

2. **Fibrosis:**
   Large amounts of tissue destruction, or damage in tissues unable to regenerate, cannot be regenerated completely by the body. Fibrous scarring occurs in these areas of damage,
forming a scar composed primarily of collagen. The scar will not contain any specialized structures, such as parenchymal cells, hence functional impairment may occur.

3. **Abscess Formation:**

A cavity is formed containing pus, an opaque liquid containing dead white blood cells and bacteria with general debris from destroyed cells.

4. **Chronic inflammation:**

In acute inflammation, if the injurious agent persists then chronic inflammation will ensue. This process, marked by inflammation lasting many days, months or even years, may lead to the formation of a chronic wound. Chronic inflammation is characterised by the dominating presence of macrophages in the injured tissue. These cells are powerful defensive agents of the body, but the toxins they release (including reactive oxygen species) are injurious to the organism's own tissues as well as invading agents. Consequently, chronic inflammation is almost always accompanied by tissue destruction.

3.1.6 **Exercise-induced acute inflammation:**

Acute inflammation of the muscle cells, as understood in exercise physiology,[39] can result after induced eccentric and concentric muscle training. Participation in eccentric training and conditioning, including resistance training and activities that emphasize eccentric lengthening of the muscle including downhill running on a moderate to high incline can result in considerable soreness within 24 to 48 hours, even though blood lactate levels, previously thought to cause muscle soreness, were much higher with level running. This delayed onset muscle soreness (DOMS) results from structural damage to the contractile filaments and z-disks, which has been noted especially in marathon runners whose muscle fibers revealed remarkable damage to the muscle fibers after both
training and marathon competition. The onset and timing of this gradient damage to the muscle parallels the degree of muscle soreness experienced by the runners.

Z-disks are the point of contact for the contractile proteins. They provide structural support for the transmission of force when the muscle fibers are activated to shorten. However, in marathon runners and those who prescribe to the overload principle to enhance their muscles, show moderate Z-disk streaming and major disruption of the thick and thin filaments in parallel groups of sarcomeres as a result of the force of eccentric actions or stretching of the tightened muscle fibers.

This disruption of the muscle fibers triggers white blood cells to increase following the induced muscle soreness, leading to the inflammatory response observation from the induced muscle soreness. Elevations in plasma enzymes, myoglobinemia, and abnormal muscle histology and ultrastructure are concluded to be associated with the inflammatory response. High tension in the contractile-elastic system of muscle results in structural damage to the muscle fiber and plasmalemma and its epimysium, perimysium, and/or endomysium. The mysium damage disrupts calcium homeostasis in the injured fiber and fiber bundles, resulting in necrosis that peaks about 48 hours after exercise. The products of the macrophage activity and intracellular contents (such as histamines, kinins, and K+) accumulate outside the cells. These substances then stimulate the free nerve endings in the muscle; a process that appears accentuated by eccentric exercise, in which large forces are distributed over relatively small cross-sectional area of the muscle.

3.1.7 Chronic inflammation and muscle loss:

Both chronic and extreme inflammation are associated with disruptions of anabolic signals initiating muscle growth. Chronic inflammation has been implicated as part of the cause of the muscle loss that occurs with aging. Increased protein levels of myostatin have been described in
patients with diseases characterized by chronic low-grade inflammation. Increased levels of TNF-α can suppress the AKT/mTOR pathway, a crucial pathway for regulating skeletal muscle hypertrophy, thereby increasing muscle catabolism. Cytokines may antagonize the anabolic effects of Insulin-like growth factor 1 (IGF-1). In the case of sepsis, an extreme whole body inflammatory state, the synthesis of both myofibrillar and sarcoplasmic proteins are inhibited, with the inhibition taking place preferentially in fast-twitch muscle fibers. Sepsis is also able to prevent leucine from stimulating muscle protein synthesis. In animal models, when inflammation is created, mTOR loses its ability to be stimulated by muscle growth.

3.1.8 Signal-to-noise theory:-

Given that localized acute inflammation is a necessary component for muscle growth, and that chronic low-grade inflammation is associated with a disruption of anabolic signals initiating muscle growth, it has been theorized that a signal-to-noise model may best describe the relationship between inflammation and muscle growth. By keeping the "noise" of chronic inflammation to a minimum, the localized acute inflammatory response signals a stronger anabolic response than could be achieved with higher levels of chronic inflammation.

3.1.9 Exercise as a treatment for inflammation:-

Regular physical activity is reported to decrease markers of inflammation[quantify], although the correlation is imperfect and seems to reveal differing results contingent upon training intensity. For instance, while baseline measurements of circulating inflammatory markers do not seem to differ greatly between healthy trained and untrained adults, long-term chronic training may help reduce chronic low-grade inflammation. On the other hand, levels of inflammatory markers (IL-6) remained elevated longer into the recovery period following an acute bout of exercise in
patients with inflammatory diseases, relative to the recovery of healthy controls. It may well be that low-intensity training can reduce resting pro-inflammatory markers (CRP, IL-6), while moderate-intensity training has milder and less-established anti-inflammatory benefits. There is a strong relationship between exhaustive exercise and chronic low-grade inflammation. Marathon running may enhance IL-6 levels as much as 100 times over normal and increases total leucocyte count and neutrophil mobilization. As such, individuals pursuing exercise as a means to treat the other factors behind chronic inflammation may wish to balance their exercise protocol with bouts of low-intensity training, while striving to avoid chronic over-exertion.

3.1.10 Targeting inflammation and Pain – Pharmaceutical focus:-

The pharmaceutical industry is one of the most profitable sectors of the Fortune 500 with profits of approximately 18% of revenue compared to a median of 5% for other industry segments. However, this market is facing increasing competitive pressure due to escalating R&D costs, shortened patent life due to the long product approval process, increased sales and marketing costs, pricing pressures, and entrance of more competitors into the industry. It is estimated that large pharmaceutical companies (or Pharma as they are generally referred to in the industry) require 3-5 new lead drug candidates (defined as New Chemical Entities or NCEs) each year to sustain double-digit growth rates. Despite the fact that R&D costs have been increasing (typically $300-500 million per NCE), the average number of NCEs have been dropping over the last decade to under one per year across the industry. Thus, there is increasing pressure on Pharma to find newer discovery and development paradigms.

Inflammation and Pain are one of the key processes linked to various diseases and disorders. There are many opportunities for designing and developing specific new drugs for inflammatory and pain responses.
Fig. 3.12 Drugs Sales Graph
3.1.11 Plants with Anti-inflammatory and Analgesic Activity:

<table>
<thead>
<tr>
<th>PLANT NAME</th>
<th>TRADITIONAL USES</th>
<th>PART USED</th>
<th>TYPE OF EXTRACT</th>
<th>EXPERIMENTAL MODELS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Albizia lebbeck</td>
<td>Barks and leaves are used to relief tooth ache, diseases of the gum, allergic disorders and bronchial asthma</td>
<td>Bark</td>
<td>Cold extraction of mixture of Petroleum ether, ethyl acetate and methanol</td>
<td>Acetic acid induced writhing, radiant heat tail flick method</td>
</tr>
<tr>
<td>Annona squamosa</td>
<td>Used to stop diarrhea, dysentery and used as a cold remedy, insecticide, expectorant</td>
<td>Bark</td>
<td>Petroleum ether</td>
<td>Acetic acid induced writhing test, carrageenan induced paw oedema</td>
</tr>
<tr>
<td>Artemisia absinthium</td>
<td>Used as tonic, stomachic, febrifuge, gastric pain, antihelmintic</td>
<td>Seed, stem</td>
<td>Methanol extract</td>
<td>Tail immersion method, carrageenan induced paw edema</td>
</tr>
<tr>
<td>Bauhinia racemosa</td>
<td>Bark, root, flower used in hemorrhoids, cough, diarrhea, menorrhagia, skin diseases</td>
<td>Stem bark</td>
<td>Methanol extract</td>
<td>Acetic acid induced writhing, carrageenan induced paw oedema</td>
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</tbody>
</table>

Table 3.1 Plants with Anti-inflammatory and Analgesic Activity
### Table 3.1 (Continued)

<table>
<thead>
<tr>
<th>PLANT NAME</th>
<th>TRADITIONAL USES</th>
<th>PART USED</th>
<th>TYPE OF EXTRACT</th>
<th>EXPERIMENTAL MODELS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carissa carandas</td>
<td>Used as stomachic, antihelmintic, antiscorbutic and useful in treatment of scabies, pruritus, intestinal worms, sour, fever</td>
<td>Root, fruit</td>
<td>Ethanol extract</td>
<td>Eddy’s hot plate, carrageenan induced rat paw edema, analgesy meter induced pain, cotton pellet induced granuloma</td>
</tr>
<tr>
<td>Cassia sieberiana</td>
<td>Traditional medicine to treat pain and Inflammation</td>
<td>Root</td>
<td>Aqueous extract</td>
<td>Acid induced writhing, carrageenan induced paw edema</td>
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<tr>
<td>Cussonia paniculata</td>
<td>Widely used against pain, inflammation, infections</td>
<td>Bark</td>
<td>Aqueous extract</td>
<td>Formalin test, carrageenan and histamine induced edema</td>
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<tr>
<td>Daphne retusa</td>
<td>Act as detumescence and acesodyne</td>
<td>Bark, Stem</td>
<td>Ethanol extract and different fractions (pet. Ether, methylene chloride, ethyl acetate)</td>
<td>Carrageenan induced paw oedema, ear oedema, acetic acid induced writhing, hot plate test</td>
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*Continued on Page No. 99-109*
### Table 3.1 (Continued)

<table>
<thead>
<tr>
<th>PLANT NAME</th>
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<th>PART USED</th>
<th>TYPE OF EXTRACT</th>
<th>EXPERIMENTAL MODELS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daphne retusa</td>
<td>Act as detumescence and acesodyne</td>
<td>Bark, Stem</td>
<td>Ethanol extract and different fractions (pet. Ether, methylene chloride, ethyl acetate and n-butanol)</td>
<td>Carrageenan induced paw oedema, ear oedema, acetic acid induced writhing, hot plate test</td>
</tr>
<tr>
<td>Desmodium triflorum</td>
<td>Used as a remedy for dysmenorrheal, muscle spasms, cough, asthma, diarrhea, dysentery, convulsions, pain</td>
<td>Whole plant</td>
<td>Methanol extract</td>
<td>λ-carrageenan induced paw edema, acetic acid induced writhing, determination of antioxidant enzymes, interleukin-1β, tumor necrosis factor and nitric oxide</td>
</tr>
<tr>
<td>Diospyros variegata</td>
<td>Use in relieving fevers and inflammation</td>
<td>Stem</td>
<td>Hexane extract</td>
<td>Acetic acid induced writhing, formalin test, tail flick method, arachidonic acid and ethyl phenylpropiolate induced rat ear edema</td>
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Continued on Page No. 100-109
<table>
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<th>PLANT NAME</th>
<th>TRADITIONAL USES</th>
<th>PART USED</th>
<th>TYPE OF EXTRACT</th>
<th>EXPERIMENTAL MODELS</th>
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</thead>
<tbody>
<tr>
<td>Garcinia hanburyi</td>
<td>Used to treat constipation, edema, bleeding</td>
<td>Gum resin</td>
<td>Ethyl acetate extract</td>
<td>Ethyl phenylpropiolate induced ear edema</td>
</tr>
<tr>
<td>Family: Guttiferae</td>
<td></td>
<td></td>
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<tr>
<td>Gloriosa superba</td>
<td>Used in rheumatism, worm infections, leprosy, ulcer, sores, tumor</td>
<td>Aerial part</td>
<td>Hydroalcoholic extract (50% v/v)</td>
<td>Acid induced writhing, eddy’s hot plate method, carrageenan induced paw edema, cotton wool granuloma model</td>
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<tr>
<td>Family: Liliaceae</td>
<td></td>
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</tr>
<tr>
<td>Glycine tomentella</td>
<td>Treating degenerative disease, joint pain, joint pain</td>
<td>Root</td>
<td>Aqueous extract</td>
<td>Acetic acid induced writhing, carrageenan induced paw edema, formalin test</td>
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<td>Family: Leguminosae</td>
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<td></td>
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<tr>
<td>Heracleum persicum</td>
<td>Purposed to reduce swelling, aid digestion and is used as tonic and aphrodisiac</td>
<td>Fruit</td>
<td>Hydroalcoholic extract</td>
<td>Acetic acid induced writhing, carrageenan induced paw edema</td>
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<td>Family: Apiaceae</td>
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Table 3.1 (Continued)

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<th>EXPERIMENTAL MODELS</th>
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<tr>
<td>Hypericum canariense</td>
<td>Used in fibromyalgia, arthritis, muscular pain and fatigue, inflammatory and painful conditions</td>
<td>Aerial part</td>
<td>Infusion, methanol extract and fractions (aqueous, butanol and chloroform fractions)</td>
<td>Acetic acid induced writhing, tail flick test, tetradecanoylphorbol acetate induced ear inflammation model</td>
</tr>
<tr>
<td>Clusiaceae</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Hypericum glandulosum</td>
<td>Used in arthritis, muscular pain and inflammatory and painful conditions</td>
<td>Aerial part</td>
<td>Infusion, methanol extract and fractions (aqueous, butanol and chloroform fractions)</td>
<td>Acetic acid induced writhing, tail flick test, tetradecanoylphorbol acetate induced ear inflammation model</td>
</tr>
<tr>
<td>Clusiaceae</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lactuca sativa</td>
<td>Plant seeds are used for relieving pain, osteodynia</td>
<td>Seed</td>
<td>Methanol/petroleum ether (70/30 v/v) extract</td>
<td>Formaline test, carrageenan induced inflammation model</td>
</tr>
<tr>
<td>Compositae</td>
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Continued on Page No. 102-109
### Table 3.1 (Continued)

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<th>TYPE OF EXTRACT</th>
<th>EXPERIMENTAL MODELS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lactuca scariola Family: Compositae</td>
<td>Used as a diuretic, antispasmodic, sedative</td>
<td>Seed, stem</td>
<td>Methanol extract</td>
<td>Tail immersion method, carrageenan induced paw oedema</td>
</tr>
<tr>
<td>Lantana trifolia Family: Verbenaceae</td>
<td>Folk medicine use as pain relievers</td>
<td>Leaf</td>
<td>Ethanol extract</td>
<td>Carrageenan, serotonin and histamine induced paw edema, acetic acid induced writhing, tail flick</td>
</tr>
<tr>
<td>Leonurus sibiricus Family: Lamiaceae</td>
<td>Plant is used in the treatment of painful menstruation, post-partum bleeding, oedema</td>
<td>Aerial part</td>
<td>Methanol extract</td>
<td>Acetic acid induced writhing, carrageenan induced paw edema</td>
</tr>
<tr>
<td>Ligularia fischeri Family: Asteraceae</td>
<td>Seed oil for sprain and rheumatism</td>
<td>Leaf</td>
<td>Ethanol extract</td>
<td>Formalin test, acetic acid induced writhing, hot plate method, carrageenan and arachidonic acid induced edema</td>
</tr>
</tbody>
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Continued on Page No. 103-109
### Table 3.1 (Continued)

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<th>PLANT NAME</th>
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<th>PART USED</th>
<th>TYPE OF EXTRACT</th>
<th>EXPERIMENTAL MODELS</th>
</tr>
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<tbody>
<tr>
<td>Mahonia oiwakensis</td>
<td>Used as bitter tonic</td>
<td>Root</td>
<td>Ethanol extract</td>
<td>Acetic acid induced writhing, formalin test. Λ-carrageenan-induced paw oedema model</td>
</tr>
<tr>
<td>Family: Berberidaceae</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Margaritaria discoidea</td>
<td>Barks are used to relief toothache, post-partum pains, relieve stomach and kidney disease, inflammation</td>
<td>Stem bark</td>
<td>Water extract</td>
<td>Carrageenan and histamine induced paw oedema, acetic acid induced writhing, formalin test.</td>
</tr>
<tr>
<td>Family: Euphorbiaceae</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Melia toosendan</td>
<td>Herbal medicine in the treatment of stomachache and many acute or chronic inflammations, as well as ascariasis.</td>
<td>Fruit</td>
<td>Ethanol extract</td>
<td>Acetic acid induced vascular permeability and Λ-carrageenan induced hind paw edema, acetic acid induced writhing and hot plate tests.</td>
</tr>
<tr>
<td>Family: Meliaceae</td>
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Table 3.1 (Continued)

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<th>TYPE OF EXTRACT</th>
<th>EXPERIMENTAL MODELS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Memecylon edule</td>
<td>In menorrhagia and heavy manstruation, and washing of eyes</td>
<td>Leaf</td>
<td>Hexane, ethyl acetate, methanol and 50% methanol fractions</td>
<td>Interleukin production, ethylphenylpropiolate induced ear edema and the writhing test</td>
</tr>
<tr>
<td>Family: Melastomataceae</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Microstilis wallichii</td>
<td>Useful in haematemesis, fever, vitiated condition of pitta and vata, dipsia, burning sensation</td>
<td>Tuber</td>
<td>Ethanolic extract (50% v/v)</td>
<td>Carrageenan and cotton palate induced granuloma, pain by analgesy meter</td>
</tr>
<tr>
<td>Family: Orchidaceae</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Newbouldia laevis</td>
<td>Used in earache, sore feet, chest pain, epilepsy, febrifuge, wound and stomach ache</td>
<td>Flower</td>
<td>Ethanolic extract</td>
<td>Formalin test, acetic acid induced writhing</td>
</tr>
<tr>
<td>Family: Bignoniaceae</td>
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<th>TYPE OF EXTRACT</th>
<th>EXPERIMENTAL MODELS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pergularia daemia</td>
<td>Used as antihelmintic, laxative, antipyretic and expectorant, and is also used to treat infantile diarrhoea and malarial intermittent fevers, inflammation</td>
<td>Root</td>
<td>Ethanolic extract</td>
<td>Eddy’s hot plate, carrageenan induced rat paw edema</td>
</tr>
<tr>
<td>Family: Apocynaceae</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Pfaffia glomerata</td>
<td>Used in fever and reduce inflammation</td>
<td>Root</td>
<td>Hydroalcoholic extract</td>
<td>Carrageenan induced paw oedema, granulomatous tissue assay, writhing test, hot plate test</td>
</tr>
<tr>
<td>Family: Amaranthaceae</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phyllanthus debilis</td>
<td>Used in sinusitis, it is a rich source of vitamin c</td>
<td>Whole plant</td>
<td>Petroleum ether extract</td>
<td>Carrageenan induced hind paw edema, chronic granuloma pouch model, tail flick model</td>
</tr>
<tr>
<td>Family: Phyllanthaceae</td>
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Table 3.1 (Continued)

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<th>PART USED</th>
<th>TYPE OF EXTRACT</th>
<th>EXPERIMENTAL MODELS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pogostemon cablin</td>
<td>Used in cold, nausea, diarrhea, headache and fever</td>
<td>Aerial part, leaf</td>
<td>Methanol extract</td>
<td>Acetic acid induced writhing, formalin test, carr-induced edema test, antioxidant study, tissue cox-2 and tnf-α determination</td>
</tr>
<tr>
<td>Family: Lamiaceae</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rheedia longifolia</td>
<td>Different plant from rheedia species used to treat inflammation, pain and infections</td>
<td>Leaf</td>
<td>Aqueous extract</td>
<td>Acetic acid induced writhing, tail flic method, hyperalgesia and pleurisy induced by lipopolysaccharide</td>
</tr>
<tr>
<td>Family: Clusiaceae</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rivea hypocrateriformis</td>
<td>Leave juice in rheumatic pain and skin disease of hair scalp</td>
<td>Leaf</td>
<td>Ethanol extract</td>
<td>Tail flick models, carrageenan induced inflammation</td>
</tr>
<tr>
<td>Family: Convolvulaceae</td>
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## Table 3.1 (Continued)

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<th>TYPE OF EXTRACT</th>
<th>EXPERIMENTAL MODELS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Saraca indica</td>
<td>To treat painful conditions, improves digestion and assimilation, alleviates excessive thirst, to kills infectious agents and in blood disease, inflammation.</td>
<td>Leaf</td>
<td>Chloroform, Methanol, water extract</td>
<td>Formalin test, tail immersion method</td>
</tr>
<tr>
<td>Smilax china</td>
<td>It is bitter, acrid, anodyne, anti-inflammatory, digestive and used in dyspepsia, flatulence, colic, skin diseases, and fever.</td>
<td>Bark</td>
<td>Aqueous extract</td>
<td>Carrageenan induced paw edema, hot plate method</td>
</tr>
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### Table 3.1 (Continued)

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<th>PART USED</th>
<th>TYPE OF EXTRACT</th>
<th>EXPERIMENTAL MODELS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spathodea campanulata</td>
<td>Plant is uses as astringent and to relief for painful inflammatory conditions</td>
<td>Leaf</td>
<td>Ethanol extract</td>
<td>Acetic acid induced writhing, tail flick method (cold induced), hot plate models, carrageenan induced oedema</td>
</tr>
<tr>
<td>Family: Bignoniaceae</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trichilia connaroides</td>
<td>Used as antihelmintic and used in stomach trouble, wound</td>
<td>Leaf</td>
<td>Chloroform extract</td>
<td>Formaline induced paw edema, acetic acid induced writhing, eddy’s hot plate method</td>
</tr>
<tr>
<td>Family: Meliaceae</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trigonella foenumgraecum</td>
<td>Used for stomach upset, swelling, rheumatism, fever and/or lowering blood sugar, and for softening the stool.</td>
<td>Seed</td>
<td>Water soluble partially purified extract (methanol extract subsequently treated with chloroform and acetone)</td>
<td>Acetic acid induced writhing, carrageenan Induced edema</td>
</tr>
<tr>
<td>Family: Leguminosae</td>
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<table>
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<th>TYPE OF EXTRACT</th>
<th>EXPERIMENTAL MODELS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Verbena tenuisecta</td>
<td>Folk medicine against diarrhea, gastrointestinal disorders, fever, pain, inflammation</td>
<td>Flower bud</td>
<td>Volatile oil isolated by hydrodistillation</td>
<td>Carrageenan induced paw edema, acetic acid induced writhing, hot plate method</td>
</tr>
<tr>
<td>Xanthium strumarium</td>
<td>Used as anodyne, antirheumatic, appetizer, diaphoretic, diuretic, emollient, laxative and sedative</td>
<td>Fruit</td>
<td>Ethanol extract</td>
<td>Acetic acid induced writhing, croton oil induced ear edema</td>
</tr>
<tr>
<td>Xeromphis spinosa</td>
<td>Used in pain, inflammation, fever and as aphrodisiac, antiemetic, carminative</td>
<td>Bark</td>
<td>Bark is extracted by ether, ethyl acetate and methanol (1:1:1)</td>
<td>Carrageenan induced paw edema</td>
</tr>
<tr>
<td>Zizyphus lotus</td>
<td>Used in inflammation, stress, tooth pain</td>
<td>Root, bark, leaf</td>
<td>Methanol extract</td>
<td>Carrageenan induced paw edema, tail-flick method</td>
</tr>
</tbody>
</table>
3.2 Literature review about the Plants selected:-

3.2.1 Argyreia speciosa

3.2.1.1 Argyreia speciosa (Linn. f.) sweet: A comprehensive review:-

V.J. Galani, B.G. Patel, N.B. Patel 2010

Department of Pharmacology, A.R. College of Pharmacy and G.H. Patel Institute of Pharmacy, Vallabh Vidyanagar, Gujarat, India

Abstract:-

Argyreia speciosa (Linn. f.) Sweet is a popular Indian medicinal plant, which has long been used in traditional Ayurvedic Indian medicine for various diseases. This plant is pharmacologically studied for nootropic, aphrodisiac, immunomodulatory, hepatoprotective, antioxidant, antiinflammatory, antihyperglycemic, antidiarrheal, antimicrobial, antiviral, nematicidal, antiulcer, anticonvulsant, analgesic and central nervous depressant activities. A wide range of phytochemical constituents have been isolated from this plant. A comprehensive account of the morphology, phytochemical constituents and pharmacological activities reported are included in view of the many recent findings of importance on this plant.

Keywords:

Anticonvulsant activity, antioxidant activity, Argyreia speciosa, central nervous depressant activity, immunomodulatory activity
3.2.1.2 Argyreia speciosa Linn. f.: Phytochemistry, pharmacognosy and pharmacological studies:

By Ashish J Modi, S S Khadabadi, U A Deokate, I A Farooqui, S L Deore, M R Gangwani

Journal of Pharmacognosy and Phytotherapy (2010), Volume: 2, Issue: 3, Pages: 34-42

Abstract:-

Many herbal remedies have been employed in various medical systems for the treatment and management of different diseases. The plant, Argyreia speciosa Linn. f. (Syn: Argyreia nervosa) belongs to family convolvulaceae has been used in different system of traditional medication for the treatment of diseases and ailments of human beings. It is reported to contain various alkaloids, glycosides, falconoid glycoside and steroids. It has been reported as antimicrobial, antidiarrhoeal, hepatoprotective, nootropic, anticonvulsant, central nervous system, hypoglycemic, antioxidant, antibacterial, antiviral, nematicidal, aphordiasic, immunomodulatory, analgesic and anti-inflammatory activity. Many isolated constituents from A. speciosa lack the reports of pharmacological activities, which support its further pharmacological studies.

Author-supplied keywords:-

Argyreia speciosa, convolvulaceae, flora, india, pharmacognosy, pharmacology, traditional, uses
3.2.1.3 Evaluation of Nootropic Effect of Argyreia speciosa in Mice:-

Joshi Hanumanthachar, Department of Pharmacognosy, SET's College of Pharmacy Kaur Navneet and Chauhan Jyotibala Department of Biotechnology, Pooja Bhagavat Memorial Mahajana's P. G. Centre

Abstract:-

Argyreia speciosa, a woody climber is widely used in ayurveda for the treatment of neurological disorders. This work researched the action of the n-hexane (n-HF), chloroform (CF), ethyl acetate (EAF) and water (WF) fractions of hydroalcoholic extract of roots of Argyreia speciosa on the central nervous system. All the fractions (100, 200 and 500 mg/kg, p.o.) were evaluated for neuropharmacological activity using spontaneous motor activity and pentobarbital-induced sleeping time in mice. Chlorpromazine was used as a positive control. Central nervous system depressant activity was observed with all the fractions as indicated by the results in which they reduced spontaneous motor activity and potentiated pentobarbital induced hypnosis in mice. These results suggest that the active principles present in the root of Argyreia speciosa may responsible for central nervous depressant activity.

Author-supplied keywords:-

Argyreia speciosa, ayurveda, hydroalcoholic, Central nervous system depressant activity, Chlorpromazine, spontaneous
3.2.1.4 Central Nervous System Activity of Argyreia Speciosa Roots in Mice:-


Abstract:-

Argyreia speciosa is a potent medicinal plant in the Indian systems of medicine. Traditionally it is used as an antibacterial, antifungal, antipyretic, etc. In the present study the hydroalcoholic extract and its acetone, chloroform and methanol fractions of the root of A. speciosa were studied for their antipyretic activity by Brewer’s yeast-induced pyrexia in rats. It was observed that the hydroalcoholic extract produced significant antipyretic activity (p < 0.05), while acetone, chloroform and methanol fraction did not.

Author-supplied keywords:-

Argyreia speciosa, potent, Indian systems, antibacterial, antifungal, antipyretic, hydroalcoholic, acetone, chloroform, fraction, methanol.
3.2.1.5 Antipyretic activity of roots of Argyreia speciosa (burm. f.):-

Bojer Sandeep Ahlawat, P.K. Mishra Sanjay College of Pharmacy, Chaumuhan, Mathura- 281406, UP, India; K. Dalal, Janta College of Pharmacy, Butana, Sonepat-131302, HR, India; Arjun Patra, College of Pharmacy, IFTM, Moradabad - 244 001, UP, India

Abstract:-

In a study the Methanolic Extract of A. speciosa root was used in pain and inflammation models. The analgesic activity of AS at the dose of (30,100, and 300 mg/kg p.o) showed significant (P<0.01) decrease in acetic acid-induced writhing, whereas ME of A. speciosa at the dose of (100, 300 mg/kg p.o) showed significant (P<0.01) increase in latency to tail flick in tail immersion method and elevated mean basal reaction time in hot plate method. The ME of the A. speciosa at doses (30, 100, and 300mg/kg) showed significant (P < 0.01) inhibition of carrageenan induced hind paw edema in rats.

Author-supplied keywords:-

Methanolic, inflammation, Analgesic, Acid-induced writhing, Latency, carrageenan induced hind paw edema.
3.2.1.6 Hepatoprotective and Antioxidant Effects of Argyreia Speciosa in Rats:

P.V. Habbu, Department of Pharmacognosy and Phytochemistry S.E.T's College of Pharmacy, S.R.Nagar, Dharwad, Karnataka, India RA Shastry, K M Mahadevan, Hanumanthachar Joshi, and SK Das PG department of Studies in chemical Sciences and Research, Kuvempu University Shankaraghatta, Shimoga, Karnataka, India

Abstract:-

Based on ethno-medical clues, the aphrodisiac property of Argeria nervosa was studied in male mice. The root, flower and, to some extent, leaf (homogenate in 2% gum acacia) of the plant showed aphrodisiac activity as evidenced by an increase in mounting behavior of mice. When different extracts of the root were tested, the activity was found in the alcohol extract (200 mg/kg; p.o, single dose). The extract, 1 hr after administration, stimulated mounting behavior of male mice in a concentration-dependent manner. The root- or flower-treated male mice also exhibited a remarkable increase in mating performance. Further, the number of males was found to be more among the pups fathered by the herbal drug-treated mice compared to those by the control mice. Thus, the plant has promising potential to be developed into an effective medicine for stimulating male sexual activity with an influence on sex ratio favoring males.

Author-supplied keywords:-
ethno-medical, aphrodisiac, Argeria nervosa, homogenate, aphrodisiac, remarkable.

3.2.1.8 Aphrodisiac activity of Argyreia Speciosa in Rats:-
CHAPTER-3

REVIEW OF LITERATURE

V.J. Galani, B.G. Patel, N.B. Patel 2010

Department of Pharmacology, A.R. College of Pharmacy and G.H. Patel Institute of Pharmacy, Vallabh Vidyanagar, Gujarat, India

Abstract:-

The root, flower and to some extent leaf of the plant showed aphrodisiac activity as evidenced by an increase in mounting behavior of mice. The plant is valuable in development of effective medicine for stimulating male sexual activity with an influence on sex ratio favoring males. A product containing a mixture of Orchis mascula, Hygrophila spinosa, Lactuca scariola, Macuna pruriens, Parmelia parlata, Argyreia speciosa, Tribulus terrestris and Leptadenia reticulate (known as Speman) was reported to improve prostatic function as assessed by the activity of maltase and by the citric acid content, with increase in the activity of amylase and maltase and a decrease in post-treatment levels of glycogen in seminal fluid. It also promotes fertility as increased sperm count, sperm motility, follicle-stimulating hormone release and synthesis. A preparation ‘Fortege’ made from Withania somnifera, Mucuna prutiens, Argyreia speciosa. Leptadenia reticulate and Anacyclus pyrethrum is used for curing common male sexual disorders. A product containing dried roots of Argyreia speciosa is effective to treat male impotence and sterility as evidenced by increase in testosterone level in alcohol-exposed rats.

Author-supplied keywords:-

Orchis mascula, Hygrophila spinosa, Lactuca scariola, Macuna pruriens, Parmelia parlata, Argyreia speciosa, Tribulus terrestris, Leptadenia reticulate.
3.2.1.9 Immunomodulatory activity of Argyreia Speciosa in Rats:-

V.J. Galani, B.G. Patel, N.B. Patel 2010

Department of Pharmacology, A.R. College of Pharmacy and G.H. Patel Institute of Pharmacy, Vallabh Vidyanagar, Gujarat, India

Abstract:-

A 95% ethanolic extract of dried root of A. speciosa was reported to stimulate both cellular and humoral immunity. Oral administration of the ethanolic extract of A. speciosa root (50, 100 and 200 mg/kg) in mice, dose dependently potentiated the delayed-type hypersensitivity reaction induced by both, sheep red blood cells and oxazolone. It significantly enhanced the production of circulating antibody titer in mice in response to sheep red blood cells. Chronic administration also significantly ameliorated the total white blood cell count and restored the myelosuppressive effects induced by cyclophosphamide.

Author-supplied keywords:-

A. speciosa, cellular and humoral immunity, oxazolone, myelosuppressive, cyclophosphamide.
3.2.1.10 Antimicrobial activity of *Argyreia Speciosa* in Rats:-

V.J. Galani, B.G. Patel, N.B. Patel 2010

Department of Pharmacology, A.R. College of Pharmacy and G.H. Patel Institute of Pharmacy, Vallabh Vidyanagar, Gujarat, India

**Abstract:**

The alcoholic extract of the leaves revealed antibacterial activity against *Staphylococcus aureus* but was inactive against *Escherichia coli*. The aqueous extract was inactive against both the bacteria. The seed oil was found to possess in vitro antibacterial activity against *Klebsiella* species, *Escherichia coli*, *Pseudomonas aeruginosa*, *Bacillus anthracis*, *Salmonella typhi*, *Salmonella paratyphi*, *Shigella boydii*, *Shigella flexneri*, *Streptococcus β-haemolyticus* and *Bacillus subtilis*. The oil was inactive against *S. aureus*. The seed oil also showed antifungal activity against *Aspergillus flavus*, *Colletotrichum capsici*, *Cryptococcus neoformans*, *Alternaria solani*, *Helminthosporium* sp., *Colletotrichum dematium*, *Aspergillus niger*, A. sydowi and *Fusarium oxysporum*. *Penicillium* sp. was found to be resistant to the oil. Hexadecanyl p-hydroxycinnamate and scopoletin isolated from the root were tested for antifungal activity against *Fusarium fusiformis*, *F. semitectum* and *Alternaria alternate*. At a concentration of 1000 ppm, both the compounds produced 100% inhibition against *Alternaria alternate*. The compounds also revealed phytotoxicity in terms of root growth inhibition of germinating wheat seeds.

**Author-supplied keywords:**

*Staphylococcus aureus*, *Klebsiella*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Bacillus anthracis*, *Salmonella typhi*, *Salmonella paratyphi*, *Shigella boydii*, *Shigella flexneri*, *Streptococcus β-haemolyticus* and *Bacillus subtilis*, *Hexadecanyl p-hydroxycinnamate*, *Helminthosporium* sp., *Colletotrichum dematium*, *Aspergillus niger*, *Fusarium fusiformis*, *F. semitectum*. 
3.2.2 Balanites aegyptiaca

3.2.2.1 Anti-inflammatory, anti-nociceptive and antioxidant activities of Balanites aegyptiaca

(L.) Delile:-


Department of Pharmacology, via Irnerio 48, Bologna University, 40126 Bologna, Italy.

Abstract:-

The anti-inflammatory and anti-nociceptive activities of methanol (ME), butanol (BE) extracts and of two new saponins isolated from Balanites aegyptiaca bark were evaluated. The study was carried out in vivo and in vitro. The samples, extracts and pure substances, were intra-gastrically administered to animals. Two different animal models, the carrageenan-induced edema, in the rat, and acetic acid-induced writhing test in mice, were adopted. Moreover, the antioxidant power of extracts, fractions and individual constituents from Balanites aegyptiaca has been evaluated in vitro, using a method based on the Briggs-Rauscher (BR) oscillating reaction. Results obtained demonstrate that both ME or BE have a significant effect at the highest dose on the number of abdominal writhes induced by acetic acid, with a 38 and 54% inhibition respectively, but no significant difference was observed for extracts at the lowest dose and for the pure compounds compared with control animals. The same extracts exhibit a significant reduction on the rat paw edema. The inhibition produced by ME is about the same (28+/-3% lowest dose, 32+/-3% highest dose) after administration. A more evident effect is obtained by BE (41+/-3% and 68+/-6% respectively) and single saponins B1 and B2 (62+/-5% and 59+/-6% respectively) after oral administration. The antioxidant activity obtained seems to be in good accordance with the
pharmacological results. The histological sections of rat paw confirm the antiflogistic activity of the plant extracts.

3.2.2.2 A review on Balanites aegyptiaca Del (desert date): phytochemical constituents, traditional uses, and pharmacological activity:-

Daya L. Chothani1, Department of Pharmacognosy, Pioneer Degree Pharmacy College, Vadodara, Gujarat, India
H.U. Vaghasiya, Department of Pharmacognosy, Sun Pharma Advanced Research Company (SPARC Ltd.) Baroda, Gujarat, India (2010)

Abstract:-

Balanites aegyptiaca Del. (Zygophyllaceae), known as 'desert date,' is spiny shrub or tree up to 10 m tall, widely distributed in dry land areas of Africa and South Asia. It is traditionally used in treatment of various ailments i.e. jaundice, intestinal worm infection, wounds, malaria, syphilis, epilepsy, dysentery, constipation, diarrhea, hemorrhoid, stomach aches, asthma, and fever. It contains protein, lipid, carbohydrate, alkaloid, saponin, flavonoid, and organic acid. Present review summarizes the traditional claims, phytochemistry, and pharmacology of B. aegyptiaca Del reported in scientific literature.

Keywords: Balanites aegyptiaca, Balanitin, desert date.
3.2.2.3 Behavioral properties of Balanites aegyptiaca in rodents:-

J Ya’u, U N Abdulmalik, A H Yaro, B A Chindo, J A Anuka, I M Hussaini Department of Pharmacology and Therapeutics, Ahmadu Bello University, Zaria, Nigeria.

Ethnopharmacological Relevance :

Balanites aegyptiaca is a native plant from the dry tropical areas of Africa and Arabia. It has been used in traditional medicine to treat psychoses, epilepsy, rheumatism and for the management of cough, liver and spleen conditions for many years. The plant is also used as antihelmintic and molluscicide.

Aim of The Study:- The present studies aimed at investigating the behavioral properties of ethanol extract of the root of this medicinal plant, which is already in common applications in the Nigerian traditional medicine.

Materials And Methods:- The intraperitoneal and oral mean lethal dose (LD(50) of the extract was determined using the Lorke's method. The preliminary phytochemical screening of the extract was carried out to identify the secondary metabolites in the extract. Furthermore, the behavioral properties of the extract were evaluated using diazepam-induced sleep, open field test, staircase test and beam walking assay all in mice.

Results:- The extract significantly (p<0.001) prolonged the duration diazepam (20mg/kg i.p)-induced sleep in mice dose dependently. However, the extract showed no significant effect on the onset of diazepam-induced sleep. In the open field test, the extract (150 and 300 mg/kg) and diazepam (0.05 mg/kg) produced a significant (p<0.05, p<0.005 and p<0.001) decrease in the number of square crossings. There was no significant effect on the number of centre square crossing following the administration of the extract. The extract (75 and 150 mg/kg) and diazepam (0.05
mg/kg) produced a significant (p<0.05) decrease in the number of rearing suggestive of sedation. In the staircase experiment there was a decrease in the number of upward step climbing as well as number of rearing suggesting anxiolytic and sedative properties of the extract. In the beam walking assay the extract did not produce any significant increase in the time taken to complete task as compared to diazepam 1mg/kg which was significant at p<0.05. Furthermore, 30 mg/kg of the extract and diazepam 1mg/kg showed significant (p<0.05) mean number of foot slips, suggesting that the central nervous system depressant activity might not necessarily due to peripheral neuromuscular blockade.

**Conclusion:** The result indicates that the extract of Balanites aegyptiaca possess biologically active compound(s) that have anxiolytic and sedative properties, which support the ethnomedicinal use of the plant as antipsychotic and antiepileptic agents.

**Keywords:** aegyptiaca; extract; diazepam; mg/kg; sleep; diazepam mg/kg; plant; behavioral; beam walk; property; diazepam-induced; staircase; anxiolytic; walk; sedative property;
3.2.2.4 Anti-inflammatory, anti-nociceptive and antioxidant activities of Balanites aegyptiaca (L.) Delile:

E. Speroni, R. Cervellati, G. Innocenti, S. Costa, M.C. Guerra, S. Dall’Acqua, P. Govoni (2005), Department of Pharmacology, via Irnerio 48, Bologna University, 40126 Bologna, Italy, Department of Chemistry G. Ciamician, Bologna University, Italy, Department of Pharmaceutical Sciences, Padova University, Italy, Department of Experimental Medicine, Section of Histology, Parma University, Italy.

Abstract:--

The anti-inflammatory and anti-nociceptive activities of methanol (ME), butanol (BE) extracts and of two new saponins isolated from Balanites aegyptiaca bark were evaluated. The study was carried out in vivo and in vitro. The samples, extracts and pure substances, were intra-gastrically administered to animals. Two different animal models, the carrageenin-induced edema, in the rat, and acetic acid-induced writhing test in mice, were adopted.

Moreover, the antioxidant power of extracts, fractions and individual constituents from Balanites aegyptiaca has been evaluated in vitro, using a method based on the Briggs–Rauscher (BR) oscillating reaction.

Results obtained demonstrate that both ME or BE have a significant effect at the highest dose on the number of abdominal writhes induced by acetic acid, with a 38 and 54% inhibition respectively, but no significant difference was observed for extracts at the lowest dose and for the pure compounds compared with control animals. The same extracts exhibit a significant reduction on the rat paw edema. The inhibition produced by ME is about the same (28 ± 3% lowest dose, 32 ± 3% highest dose) after administration. A more evident effect is obtained by BE (41 ± 3% and 68 ± 6%
respectively) and single saponins B1 and B2 (62 ± 5% and 59 ± 6% respectively) after oral administration. The antioxidant activity obtained seems to be in good accordance with the pharmacological results. The histological sections of rat paw confirm the antiflogistic activity of the plant extracts.

**Abbreviations:**

ME-methanolic extract; BE- butanolic extract; B1- Balanin 1; B2, Balanin 2; BR-Briggs–Rauscher reaction; TEAC- trolox equivalent antioxidant capacity.

**Keywords:**

Balanitesaegyptiaca extracts; Saponins; Anti-inflammatory effects; Anti-nociceptive effects;

Antioxidant activity.
3.2.2.5 In vitro immunomodulating properties of selected Sudanese medicinal plants:

W.S. Koko, M. Ahmed Mesaik, S. Yousaf, M. Galal, M. Iqbal Choudhary (2008),

Medicinal and Aromatic Plants Research Institute, National Center for Research, P.O. Box 2404, Khartoum, Sudan,

Dr. Panjwani Center for Molecular Medicine and Drug Research, International Center for Chemical and Biological Sciences, University of Karachi, Karachi - 75270, Pakistan,

H.E.J. Research Institute of Chemistry, International Center for Chemical and Biological Sciences, University of Karachi, Karachi - 75270, Pakistan.

Abstract:-

Ethanolic extracts of 23 medicinal plants, commonly used in Sudanese folk medicines against infectious diseases, were investigated for their immunomodulating activity using luminol/lucigenin-based chemiluminescence assay. Preliminary screenings on whole blood oxidative burst activity showed inhibitory activities of 14 plant extracts, while only one plant, Balanitesaegyptiaca fruits exhibited a proinflammatory activity. Further investigation was conducted by monitoring their effects on oxidative burst of isolated polymorphonuclear cells (PMNs) and mononuclear cells (MNCs) by using two different phagocytosis activators (serum opsonizing zymosan-A and PMA). Results obtained showed that the fruits and barks of Acacia nilotica, and leaves and barks of Khaya senegalensis, possess average inhibitory effects in the range of 70.7, 67.1, 69.5 and 67.4% on both types of phagocytes (PMNs and MNCs), respectively, at a 6.25 μg/mL concentration. Moderate inhibitory activity (52.2%) was exerted by the aerial parts of Xanthium brasiliicum, while the rest of the plants showed only a weak inhibitory activity. The inhibition of oxidative burst activity was found to be irreversible in most of the extracts, except for Peganum harmala, Tephrosia apollinea,
Tinospora bakis, and Vernonia amygdalina. Interestingly, the fruits of Balanites aegyptiaca exhibited a moderate proinflammatory effect (37–40.4% increases in ROS level compared to the control) at 25–100 μg/mL concentration in the case of whole blood along with PMNs phagocyte activity. The Tinospora bakis extract showed proinflammatory response at a low concentration (6.25 μg/mL) during activation with PMA. None of these extracts affected PMNs viability (90–98%) upon 2 h incubation, except of the ethanolic extracts of Acacia nilotica fruits and Balanites aegyptiaca barks.

**Abbreviations:-**

DMSO - dimethylsulfoxide; HBSS - Hanks Balance Salts Solution; HCV - hepatitis C virus; HIV - human immunodeficiency virus; IC₅₀ - inhibitory concentration 50%; ICCS - International Center for Chemical Sciences, University of Karachi, Pakistan; LSM - Lymphocytes Separation Medium; MAPRI - Medicinal and Aromatic Plants Research Institute, Khartoum, Sudan; MNCs - mononuclear cells; NADPH, reduced form of nicotinamide adenine dinucleotide phosphate; P, probability (statistical evaluation); PKC - protein kinase C; PMA - phorbol 12-myristate 13-acetate; PMNs - polymorphonuclear cells; RAW 264.7 - mouse leukaemic monocyte macrophage cell line; RBCs - red blood cells; RLU - reading per luminometer unit; ROS - reactive oxygen species; SOZ - serum opsonizing zymosan-A; TB - trypan blue; TNF-α - tumor necrosis factor alpha.

**Keywords:-**

Sudanese medicinal plants; Immunomodulation; Chemiluminescence; Oxidative burst.
3.2.2.6 Anti-Inflammatory Activity of Aerial part of Balanites aegyptiaca (L.) Del against

Carrageenan induced Paw Oedema:-

T. Mayba Gnana Suky, Department of Botany, Holy Cross College, Tiruchirapalli, Tamil nadu.
B. Parthipan, PG and Research Department of Botany, ST. Hindu College, Nagercoil, Tamil Nadu, India,
B. Parthipan, PG and Research Department of Botany, Scott Christian College, Nagercoil, Tamil Nadu, India,
C. Kingston and V.R. Mohan, Ethnopharmacology unit, Research Department of Botany, V.O.Chidambaran College, Tuticorin-628008. Tamil Nadu, India

Abstract:-

Balanites aegyptiaca (L.) Del has been used in a variety of folk medicines in India and Asia. In the present study, aerial part of Balanites aegyptiaca (L.) Del was extracted with ethanol and evaluate for their anti-inflammatory activity in rat using a carrageenan induced paw oedema method. Ethanol extract exhibits potent anti-inflammatory activity at 200 mg/kg 3 hrs. after administration in compare with reference standard, Indomethacin. Observed pharmacological activities provide the scientific basis for the folkloric use of the plant in treating acute inflammation.

Key Words:- Balanites aegyptiaca, Anti-inflammatory, Carrageenan.

Introduction:-

Balanites aegyptiaca (L.) Del belongs to the family Balanitaceae. It is an evergreen xerophytic tree of tremendous medicinal importance. It is distributed throughout the dried parts of India. B.aegyptiaca has been used in a variety of folk medicines in India and Asia. Various parts of the plants are used in Ayurvedic and other folk medicines for the treatment of different ailments such as syphilis, jaundice, liver and spleen problems, epilepsy, yellow fever and the plant also has
insecticidal, anthelmintic, antifeedant, molluscicidal and contraceptive activities. Significant anti-inflammatory activity was evaluated in methanolic and ethanolic extracts of the bark of *B. aegyptiaca* in two different animal models. A wide variety of plants with potent anti-inflammatory activity are used in folk medicines. The search for safe and effective anti-inflammatory drugs through the evaluation of medicinal plants known to be used in the treatment of inflammation disorder is continued even today. The purpose of the present study was to evaluate the possible anti-inflammatory activity of aerial part of ethanol extract of *B. aegyptiaca* using the carrageenan induced oedema test. Producing carrageenan-induced inflammation in the rat hind paw (acute inflammation) is a useful method for screening potential anti-inflammatory agents.

**Materials and Methods:**

**Plant material:** The aerial part of *Balanites aegyptiaca* (L.) Del. collected from Vadavalli, Coimbatore, Tamil Nadu. The plant was identified with the help of local flora and authenticated in Botanical Survey of India, Southern Circle, Coimbatore, Tamil Nadu, India. A voucher specimen was deposited in Ethnopharmacology unit, Research Department of Botany, V.O.Chidambaram College, Tuticorin, Tamil Nadu.

**Preparation of plant extract for anti-inflammatory activity:**

The aerial part of *Balanites aegyptiaca* (L.) Del. were cut into small pieces, washed, shade dried at room temperature and the dried aerial parts was powdered in a Wiley mill. Hundred grams of aerial part powdered was packed in a Soxhlet apparatus and extracted with ethanol. The ethanol extracts were concentrated in a rotary evaporator. The concentrated ethanol extract was used for anti-inflammatory activity.
Animals:

Adult Wistar albino rats of either sex (150-200g) were used for present investigation. Animals were housed under standard environmental conditions at temperature (25±2°C) and light and dark (12:12 h). Rats were feed standard pellet diet (Goldmohur brand, MS Hindustan lever Ltd., Mumbai, India) and water ad libitum.

Acute toxicity study:

For toxicity studies, six Albino rats of either sex were administered orally with the test substance in the range of doses 200-2000 mg/kg and the mortality rates were observed after 72h. The ethanol extract of Balanites aegyptiaca (L.) Del. has shown no mortality at 2000 mg/Kg. Therefore 2000mg/Kg dose was considered as LD50 cut off dose (safe dose). So 1/20 and 1/10 of that were selected (100 and 200 mg/Kg) for the experiment as sub maximal and maximal dose.

Anti-inflammatory activity Carrageenan-induced hind paw oedema :

Albino rats of either sex weighing 150-200 grams were divided into four groups of six animals each. The dosage of the drugs administered to the different groups was as follows. Group I - Control (normal saline 0.5 ml/Kg), Group II and III - Balanites aegyptiaca (100 mg/kg and 200 mg/kg, p.o.) respectively and Group IV - Indomethacin (10 mg/kg, p.o.). All the drugs were administered orally. After one hour of the administration of the drugs, 0.1 ml of 1% W/V carrageenan solution in normal saline was injected into the subplantar tissue of the left hind paw of the rat and the right hind paw was served as the control. The paw volume of the rats were measured in the digital plethysmograph (Ugo basile, Italy), at the end of 0 min., 60 min., 120 min., 180min., 240min., 360min., and 480min. The percentage increase in paw oedema of the treated groups was compared with that of the control and the inhibitory effect of the drugs were studied. The relative potency of the drugs was calculated based upon the percentage inhibition of the inflammation.
CHAPTER-3

REVIEW OF LITERATURE

Percentage inhibition:-

\[
\text{Control (\% increase – Test (\% increase in paw in paw volume in 3rd hour) volume in 3rd hour)} \\
\frac{\text{-----------}}{\text{-----------} \times 100} \\
\text{Control (\% increase in paw volume in 3rd hour)}
\]

Statistical analysis:-

The data were analyzed using student’s t-test statistical methods. For the statistical tests a p values of less than 0.01 and 0.05 was taken as significant.

Results:-

In the present study, the anti-inflammatory activity of ethanol extract of aerial part of Balanites aegyptiaca was assayed in Albino rats using carrageenan-induced rat paw oedema (acute inflammation) method. Table 1 shows that the anti-inflammatory activity of ethanol extract of aerial part of Balanites aegyptiaca significantly inhibited the rat paw oedema at 3rd hr post carrageenan were 57.92% and 64.46% for 100 and 200 mg/kg of ethanol extract of Balanites aegyptiaca respectively. This results indicated that ethanol extracts with a dose of 200mg/kg body weight showed a maximum anti-inflammatory activity is similar to the reference drug indomethacin, which showed 56.86% of inhibition.

Discussion:-

Oedema represents the early phase of inflammation in carageenan induced paw oedema and is the simplest and most widely used acute inflammatory model for studying anti-inflammatory agents. Carrageenan-induced inflammation is useful in detecting orally active anti-inflammatory agents. The development of carrageenan-induced oedema is believed to be biphasic. The initial phase is attributed to the release of histamine and serotonin.
The oedema produced at the peak 3hr is thought to be due to the release of Kinin-like substances, especially bradykinin. The second phase of oedema is due to the release of prostaglandins, protease and lysosomes and it is sensitive to most anti-inflammatory drugs. This study reports for the first time to our knowledge that ethanol extract of aerial part of Balanites aegyptiaca has anti-inflammatory activity. Acute toxicity study was observed that the ethanol extract of aerial part of Balanites aegyptiaca did not show any behavioral changes or mortality even at a dose of 2000 mg/kg and indicative of the safety of this extract. Further studies may reveal the exact mechanisms of action responsible to treat for the analgesic and anti-inflammatory activities. Though the study has highlighted the anti-inflammatory activities of ethanol extract of aerial part of Balanites aegyptiaca could be a potential new natural source as well as scientific proof of its ethnopharmacological use in inflammatory disorders.
3.3.3 Gloriosa superba

3.3.3.1 Isolation and anti-inflammatory activity of colchicinoids from Gloriosa superba seeds:

C.S. Joshi, E. Sanmuga Priya, C.S. Mathela

Phytochemistry Laboratory, Chemistry Department, D.S.B. Campus, Kumaun University, Nainital, India

Abstract:

Gloriosa superba L. (Liliaceae) seeds, known as “kalihari” (Hindi), were phytochemically investigated for colchicine (well known for gout treatment) and other related alkaloid content. Colchicine, 2-demethylcolchicine, 3-demethylcolchicine, and N-formyl-N-deacetylcolchicine were alkaloids isolated from the seeds. The isolated samples have been standardized for their purity with respect to the reference standard using HPLC. The structures were confirmed by NMR spectroscopy and were analyzed by spiking them along with colchicine reference by HPLC. The purity of colchicine, 2-demethylcolchicine, 3-demethylcolchicine and N-formyl-N-deacetylcolchicine were 99.82, 96.78, 98.71, and 98.13% respectively. The compounds were subjected to an anti-inflammatory study by using the formaldehyde inflammagen-induced inflammation model. Oral administration of colchicine at 2, 4, and 6 mg/kg body weight resulted in 48.9, 68.7, and 79.1% inhibition respectively, while 30.9% inhibition was seen in the phenylbutazone 100 mg/kg treated group once daily for a period of 4 days. The results clearly indicated that the colchicine is more effective as an anti-inflammatory agent compared with phenylbutazone, the standard drug used in the study, whereas the oral administration of 6 mg/kg body weight of 2-demethylcolchicine, 3-demethylcolchicine and N-formyl-N-deacetylcolchicine...
showed very poor activity (41.6, 40.4, and 41.1% activity respectively).

Keywords:-

Gloriosa superba, colchicinoids, anti-inflammatory activity, paw edema.

3.3.3.2 Critical review on medicinally potent plant species: Gloriosa superba:-

Sonali Jana, G.S. Shekhawat, Department of Bioscience and Biotechnology, Banasthali University, Banasthali-304022, Rajasthan, India (2010)

Abstract:-

Gloriosasuperba L. is a perennial climber and is used as an ayurvedic medicinal herb to cure diseases in various parts of Africa and Southeast Asia. The plant was under threatened category due to its imprudent harvesting from wild as it is extensively used by medicinal industries for its colchicine content. It also faces a low seed set problem, but due to its industrial demand it is now under cultivation. The plant is used to cure arthritis, gout, rheumatism, inflammation, ulcers, bleeding piles, skin diseases, leprosy, impotency, snakebites, etc. Various compounds have been isolated from the plant parts mainly tubers and seeds, viz colchicine, colchicoside (its semi-synthetic derivative — thiocolchicoside), superbine, gloriosine, lumicolchicine, 3-demethyl-N-deformyl-N-deacetylcolchicine, 3-demethylcolchicine, N-formyl deacetylcolchicine. In the present review, we have summarized the information concerning the occurrence, botanical description, ethanopharmacology, medicinal uses, biological activities and toxicological studies on this plant.

Keywords:-

Gloriosasuperba; Biological activities; Colchicine; Ethanopharmacology; Medicinal plant; Phytochemistry.
3.3.3.3 Effect of the Aqueous Extract of Gloriosa superba Linn (Langli) Roots on Reproductive System and Cardiovascular Parameters in Female Rats:

Arati A Malpani¹, Urmila M Aswar², Shiv K Kushwaha², GN Zambare² and SL Bodhankar²*

¹Department of Pharmacology, HKES’s College of Pharmacy, Sedam Road, Gulbarga 585105, ²Department of Pharmacology, Bharati Vidyapeeth University, Poona College of Pharmacy, Erandewane, Paud Road, Pune411038, India

Abstract:-

Purpose:

Gloriosa superba Linn (liliaceae) has been used to induce labor in the traditional Indian system of medicine. The objective of the study was to evaluate the activity of the aqueous extract of Gloriosa superba (AL) root on the female reproductive system of rat.

Methods:

The aqueous extract of Gloriosa superba was prepared by simple maceration. Phytochemical analysis as well as toxicity (in mice) and antifertility studies, uterotrophic assay, duciduoma model, uterotonic assessment in-vitro and in-vivo of aqueous extract was carried out in rats. Oxytocin was used as the uterotonic reference standard. The effect of the extract on cardiovascular parameters was also evaluated.

Results:

Phytochemical analysis shows presence of flavonoids, tannins, alkaloids, and glycosides in the aqueous extract of Gloriosa superba. The extract yield was 6 % and was found to be was safe at a
dose as high as 550 mg/kg body weight. Antifertility study showed early abortifacent activity. No increase in uterus and ductual weight was observed. Both the reference (oxytocin) and the extract produced dose-dependent contractions but the extract had no effect on heart parameters and blood pressure.

**Conclusion:** The aqueous extract of Gloriosa superba showed oxytocic activity and early abortifacent activity which may be due to the presence of alkaloids such as colchicine. This provides justification for its use in traditional medicine.

**Keywords:** Abortifacent activity; Blood pressure; Gloriosa superba; Oxytocic activity
3.3.3.4 Hepatoprotective efficacy of Gloriosa superba against paracetamol treated experimental rats- An in vivo study:

Abstract:

Paracetamol was chosen to induce hepatotoxicity in rats. Gloriosa superba tubers were extracted and used for the treatment against paracetamol induced toxicity. In this study, the animals were divided into three groups comprising of six animals each. Group I served as a control, group II animals were administered with paracetamol (200 µg/kg) orally for 10 days, group III animals were received Gloriosa superba tubers aqueous extract (500 mg/kg/bw/po) for 5 days followed by paracetamol (200 µg/kg) orally for 2 days. Hepatic marker enzymes such as Aspartate transaminase (AST), Alanine transaminase (ALT), Alkaline phosphatase (ALP), Acid phosphatase (ACP), Lactate Dehydrogenase (LDH), and Enzymic and Non-Enzymic Antioxidants such as Ascorbic acid, Reduced glutathione (GSH), Catalase, Glutathione Peroxidase (GPx) were analyzed in all groups of animals. From this study, it can be concluded that the extract of Gloriosa superba possess anti-hepatotoxic action against paracetamol toxicity.

Keywords: Hepatotoxicity, Paracetamol, Gloriosa superba

Introduction:

Gloriosa superba is one of the oldest species from ancient time. Being native form Indian specially Southern India it is known as glory lily and climbing lily- in English; Karihari- in Hindi; Langli- in Sanskrit. Antimicrobial and in vitro antioxidant activities of the plants were reported. Analgesic and anti-inflammatory properties of Gloriosa superba were determined [1]. Gloriosa superba L. is a medicinal plant belonging to the family Liliaceae. Seeds and tubers contain alkaloids such as colchicine and colchicoside, which are used to treat gout and rheumatism (Trease and Evans, 1983).
In the Indian systems of medicine, the tubers are used as tonic, antiperiodic, antihelmenthic, and also against snake bites (Gupta et al., 2005). The plant is known as ‘Kalihari’ in Hindi, ‘Manthori khizangu’ in Malayalam, and ‘Kazhappai kizhangu’ in Tamil. The species has been domesticated more recently following its overexploitation in the natural habitats (Sivakumar and Krishnamurthy, 2002).

Paracetamol is a common antipyretic agent, which is safe in therapeutic doses but can produce fatal hepatic necrosis in man, rats and mice with toxic doses (Mitchell, 1993). Protection against paracetamol – induced toxicity has been used as a test for potential hepatoprotective activity by several investigators (Visen, 2001). Based on the beneficial properties of Gloriosa superba tuber extract as a hepatoprotectant against paracetamol induced hepatotoxicity in experimental rats and delineate the mechanism of action by studying the alteration in enzymic activities and antioxidant status.

Materials and methods:-

Collection of plant material:-

The tubers of Gloriosa superba were collected from ayurveda shop of Tharapuram district of Tamilnadu, India.

Preparation of Aqueous extract:-

The tubers were shade dried at room temperature and powdered, weighed 10gm of plant powder and dissolved in 100ml of distilled water and mixed well and the extract was filtered through Whatmann No. 1 filter paper. This extract was used for further analysis.
Preliminary Phytochemical analysis of aqueous extract of Gloriosa superba:-

Qualitative phytochemical analysis of aqueous extract of Gloriosa superba tubers was performed by the method of Peach and Tracy, 1955.

Animals used:-

The female Wistar strains albino rats weighing between 100-150 gm were obtained from Small Animal Breeding Center, Kerala Agricultural University, Trissur.

Experimental setup:-

Rats were divided into three groups comprising of six animals each.

Group I – Normal healthy rats were served as Control.

Group II – Administered paracetamol (200μg/kg/) orally for 2 days.

Group III – Received Gloriosa superba (500mg/kg/bw/po) for 5 days followed by paracetamol (200 μg/kg/).orally for 2 days.

Preparation of Tissue Homogenate:-

At the end of experimental period, the animals were killed by cervical decapitation. Blood was collected, Serum separated and used for determination of biochemical constituents. Liver was removed and washed with ice-cold saline. A 10 % homogenate of the washed kidney tissues were prepared in 0.01 M Tris-HCL buffer, pH 7.4. The homogenate was centrifuged for 30min and the supernatant was used for the assay of enzymes.
Assay of hepatic marker enzymes and Serum Bilirubin:-

Hepatic marker enzymes such as Aspartate Transaminase (AST) and Alanine Transaminase (ALT) [Reitman and Frankel, 1957], Alkaline phosphatase (ALP) and Acid Phosphatase (ACP) [King, 1965a], lactate Dehydrogenase (LDH) [King, 1965b] and Serum Bilirubin [Malloy and Evlen, 1988].

Results And Discussion:-

I. Phytochemical Analysis:-

The phytochemicals present in Gloriosa superba tubers is presented in table 1. This shows that aqueous extract contains Alkaloids, Carbohydrates, Proteins, Thiols.

II. Hepatoprotective activity of Gloriosa superba tubers:-

1. Estimation of serum bilirubin:-

Bilirubin is one of the most useful clinical markers to diagnosis the severity of necrosis and its accumulation is a measure of binding, conjugation and excretory capacity of hepatocyte. Table 2 represents the estimation of serum bilirubin in control and experimental animals. From the table 2, it is found that the level of serum bilirubin was significantly increased in serum of Paracetamol treated group II rats. After the treatment with plant extract, the level of serum bilirubin reverted to near normal range in group III rats. Thus from the above result it was evident that the activity of bilirubin in serum was brought back to normal range on treatment with plant extract in paracetamol treated rats.

2. Assay of hepatic marker enzymes:-

The activities of these enzymes are usually raised in acute hepatotoxicity or mild hepatocellular injury, but tend to decrease with prolonged intoxication due to damage in liver
(Cornelius, 1979; Jens and Hanne, 2002). From the table 3, it is found that the activity of enzyme was significantly increased in Paracetamol treated hepatic damaged rats. After the treatment with plant extract the value showed near normal in group III rats which showed significant hepatoprotective activity. Thus from the above result it was evident that the activity of AST and ALT was brought back to normal range on treatment with plant extract in paracetamol treated rats.

3. Assay of hepatic membrane and lysosomal marker enzyme:-

ALP is present in all tissues throughout the body, but it is particularly concentrated in the liver, bile duct, kidney, bone and placenta. Acid phosphatase (ACP) is a phosphatase, which acts to liberate free phosphate groups from other molecules. It is basically a phospho monoesterase. It is stored in lysosomes and functions when these fuse with endosomes, which are acidified while they function. Therefore, it has an acidic pH as optimum. The activity of enzymes were significantly increased (p<0.01) in serum of Paracetamol treated rats. After the treatment with plant extract the value showed near normal in group III rats, which proved the medicinal value of the plant. Thus from the above result it was evident that the activity of ALP and ACP were brought back to normal range on treatment with tuber extract in Paracetamol treated rats.

4. Assay of hepatic cytosolic marker enzyme:-

LDH is an enzyme found in the cells of many body tissues including the heart, liver, kidneys, skeletal muscle, brain, red blood cells and lungs. It is responsible for converting muscle lactic acid into pyruvic acid, an essential step in producing cellular energy. Table 5 shows that the activity of enzyme was significantly decreased (p<0.01) in serum of Paracetamol treated rats. After the treatment with plant extract the value showed near normal in group III rats, which proved the medicinal value of the plant.
Thus from the above result it was evident that the activity of LDH was brought back to normal range on treatment with tuber extract in Paracetamol treated rats.

**Summary And Conclusion:-**

Liver is a major metabolic organ involved in the synthesis of large number of metabolites. It contains large amount of marker enzymes. The level of serum bilirubin was found to be increased during paracetamol toxicity. The activity of hepatic marker enzymes such as AST, ALT, ALP, ACP and LDH was found to be increased in group II rats due to paracetamol toxicity. The level of the hepatic marker enzymes were reverted to near normal might be due to action of phytonutrients of Gloriosa superba tubers. From the present study, it can be concluded that the extract of Gloriosa superba possess anti-hepatotoxic action against paracetamol toxicity.
3.3.3.5 Investigation Of Anti-Inflammatory Properties of Swertia Chirayta And Gloriosa Superba

Abhishek Mathur1, Satish K. Verma3, Santosh K. Singh4, Deepika Mathur5, GBKS Prasad2, V.K. Dua1

1National Institute of Malaria Research, Sector-III, Ranipur, BHEL, Hardwar (U.K), India
2Jiwaji University, Gwalior (M.P), India
3Sai Institute of Paramedical & Allied Sciences, Dehradun (U.K), India
4Gayatri Institute of Biomedical Science, Dehradun (U.K), India
5Jawaharlal Nehru Cancer Hospital & Research Center, Bhopal (M.P), India

Abstract:

Gloriosa superba (Liliaceae) is one of the oldest ingredients of species from ancient time. Tubers roots and seeds are two most important part of glory lily used for variety of purpose. Swertia chirata (Gentianaceae) is widely used in India to treat fever and malaria. It is also used to treat liver diseases. The whole plant methanol and aqueous extracts of Swertia chirayta possessed maximum anti-inflammatory activity in a dose dependent manner i.e 50 mg/kg and 100 mg/kg in carrageenan induced animal models. Further screening of the potent extracts of the plant confirmed the presence of xanthone (1, 5- dihydroxy-3, 8-dimethoxy xanthone, m.p.1850C, yellowish crystalline needles from methanol) was obtained. The structure of the fraction was confirmed by spectral analysis (UV, IR, NMR). The methanol and aqueous extracts of tubers of Gloriosa superba also possessed good anti-inflammatory in a dose dependent manner i.e 100 mg/kg and 200 mg/kg in carrageenan induced animal models. Further screening of the extracts confirmed the presence of colchicines in the extracts. The present study thus revealed the presence of potent anti-inflammatory drugs in these plants.
Keywords: Gloriosa superba, Swertia chirayta, Methanol extracts, Xanthones, Colchicines, Anti-inflammatory activity

Introduction:

Traditional system of medicine is found to have utilities as many accounts. Due to population rise adequate supply of drug and high cost of treatment in side effect along with drug resistance has been encountered in synthetic drugs, which has lead to an elevated emphasis for the use of plants to treat human diseases. The affordability of herbals has also drawn the attraction towards their use. India is one of the oldest civilizations which is known for rich repository of medicinal plants. Gloriosa superba is one of the oldest species from ancient time. Being native form Indian specially Southern India it is known as glory lily and climbing lily- in English; Karihari- in Hindi; Langli- in Sanskrit. Antimicrobial and in vitro antioxidant activities of the plants were reported. Analgesic and anti-inflammatory properties of Gloriosa superba were determined. Larvicidal and antipox viral potential of the plants were reported. Swertia chirayta is considered the most important for its medicinal properties. The bitterness, antihelmintic, hypoglycemic and antipyretic properties are attributed to amarogentin (most bitter compound isolated till date), swerchirin, swertiamarin and other active principles of the herb. Herbal medicines such as Ayush-64, Diabecon, Menstrual syrup and Melicon V ointment contain chirayta extract in different amounts for its antipyretic, hypoglycemic, antifungal and antibacterial properties. Anti-inflammatory activities of Swertia chirayta were determined. In the present study different solvent extracts of tubers of Gloriosa superba and whole plant extracts of Swertia chirayta were screened for their anti-inflammatory activity in carrageenan induced animal models.
Materials and Methods:

Plant material:

The authenticated sample was collected from Forest Research Institute, Dehradun (U.K), India and was further confirmed in Botanical Survey of India (BSI), Dehradun. Voucher specimens have been deposited in BSI, Dehradun, India.

Preparation of plant extracts:

The method was adopted for preparation of plant extracts with little modifications. Briefly four 20 g portions of the powdered plant material were soaked separately in 100 ml of water, hexane, methanol and petroleum ether for 72 h. Each mixture was stirred after every 24 h using a sterile glass rod. At the end of extraction, each extract was passed through Whatmann filter paper no1 (Whatmann, England). The filtrate obtained were concentrated in vacuo using rotary evaporator at 30\(^{\circ}\)C.

Determination of in vivo anti-inflammatory activity Animals:

Male albino rats (180–200 g) were used taking into account international principles and local regulations concerning the care and use of laboratory animals [10]. The animals had free access to a standard commercial diet and water ad libitum and were kept in rooms maintained at 22 ± 1\(^{\circ}\)C with a 12-h light/dark cycle. The institutional animal ethical committee has approved the protocol of the study.

Carrageenan-induced edema in rats:

6 Groups of five animals each were used for each of the plants. Paw swelling was induced by sub-plantar injection of 0.1 ml 1% sterile carrageenan in saline into the right hind paw. The solvent extracts of Gloriosa superba and Swertia chirayta at dose of 50, 100 and 200 mg/kg were
administered orally 60 minutes before carrageenan injection. Aspirin (10 mg/kg) was used as reference drug. Control group received the vehicle only (10 ml/kg). The inflammation was quantified by measuring the volume displaced by the paw, using a plethysmometer at time 0, 1, 2, 3, and 4 h after carrageenan injection. The difference between the left and the right paw volumes (indicating the degree of inflammation) was determined and the percent inhibition of edema was calculated in comparison to the control animals.

Statistical analysis:-

The results were expressed as mean ± S.D. Statistical significance was determined by analysis of variance and subsequently followed by Turkey’s tests. P values less than 0.05 were considered as indicative of significance. The analysis was performed using INSTAT statistical software.

Results and Discussion:-

The anti-inflammatory effects of the solvent extracts of Swertia chirayta and Gloriosa superba in carrageenan-induced edema in rat’s hind paws are reported. The anti-inflammatory activities of both the plant extracts were found to have effect in dose-dependent manner. There was a gradual increase in edema paw volume of rats in the control groups. However, in the test groups, methanol extracts of Swertia chirayta possessed maximum anti-inflammatory activity in a dose dependent manner i.e 50 mg/kg and 100 mg/kg in carrageenan induced animal models in comparison to that of aqueous extracts. The same results were found in case of Gloriosa superba, methanol extracts possessed maximum anti-inflammatory activity in a dose dependent manner i.e 100 mg/kg and 200 mg/kg in carrageenan induced animal models in comparison to aqueous extracts. The results showed that methanol fractions of the whole plant of Swertia chirayta causes significant reduction in inflammation i.e 92 % (100 mg/kg) followed by crude aqueous extract i.e 85 % (100 mg/kg) compared to standard anti-inflammatory drug aspirin i.e 68.62% (25 mg/kg).
The dose of 200 of solvent extracts of the plant, Swertia chirayta was found to be lethal dose for carrageenan induced mice and most of rats lead to death. In case of Swertia chirayta extracts, the values of reduction in paw volume, 0.10 ± 0.002, 0.12 ± 0.002 and 0.14 ± 0.002 were found significantly of methanol extract, aqueous extract and aspirin, respectively at 4 h after carrageenan administration. The methanol fractions of the tubers of Gloriosa superba causes significant reduction in inflammation i.e 85 % (200 mg/kg) followed by crude aqueous extract i.e 76 % (200 mg/kg) compared to standard anti-inflammatory drug aspirin i.e 68.62% (25 mg/kg). In case of Gloriosa superba extracts, the values of reduction in paw volume, 0.11 ± 0.002, 0.13 ± 0.002 and 0.14 ± 0.002 were found significantly of methanol extract, aqueous extract and aspirin, respectively at 4 h after carrageenan administration. There was no reduction in inflammation found in case of rats treated with petroleum ether and hexane extracts of both the plants. The present study provides evidence that the methanol fraction and aqueous extract of Swertia chirayta and Gloriosa superba acts as potent anti-inflammatory agent in dose-dependent manner in rats in acute inflammation model. Our results are found to be correlated with the previous studies. Further studies on the isolation and identification of the potent extracts confirmed the presence of Xanthones (in Swertiachirayta) and Colchicines (in Gloriosa superba) in the plant extracts responsible for anti-inflammatory activity. The active principles of the extracts were re-again screened for their anti-inflammatory activity.

Conclusion:-

The present study thus confirmed that Swertia chirayta and Gloriosa superba can be used as potent anti-inflammatory agents. The active principles of these plant(s) extracts must be further optimized in a specific amount of dose using different inflammation induced animal models. These potent compounds can be further utilized to formulate a new potent anti-inflammatory drug.
3.3.3.5 Antioxidant activity of *Gloriosa superba* against paracetamol induced toxicity in experimental rats:

Mrs. Indhumathi.T*, Ms. Sreetha erattarakkal (2011)

Department of Biochemistry, Dr.N.G.P Arts and Science College, Coimbatore-48.

**Abstract:-**

Paracetamol was chosen to induce hepatotoxicity in rats. Gloriosa superba tubers were extracted and used for the treatment against paracetamol induced toxicity. In this study, the animals were divided into three groups comprising of six animals each. Group I served as a control, group II animals were administered with paracetamol(200 μg/kg) orally for 10 days, group III animals were received Gloriosa superba tubers aqueous extract (500 mg/kg/bw/po) for 5 days followed by paracetamol(200 μg/kg) orally for 2 days. Level of LPO was found to be increased during paracetamol intoxication with concomitant decrease in the activity of enzymic and non-enzymic antioxidants. The antioxidant enzyme levels were reverted to near normal in Group III rats which results the antioxidant activity of Gloriosa superba.

**Key words:** Gloriosa superba, Antioxidant, Lipid per oxidation, Paracetamol.

**Introduction:**

Gloriosa superba is one of the oldest species from ancient time. Being native form Indian specially Southern India it is known as glory lily and climbing lily- in English; Karihari- in Hindi; Langli- in Sanskrit. Antimicrobial and in vitro antioxidant activities of the plants were reported. Analgesic and anti-inflammatory properties of Gloriosa superba were determined. Gloriosa superba L. is a medicinal plant belonging to the family Liliaceae. Seeds and tubers contain alkaloids such as colchicine and colchicoside, which are used to treat gout and rheumatism. In the Indian systems of medicine, the tubers are used as tonic, antiperiodic, antihelmenthic, and also against snake bites.
The plant is known as ‘Kalihari’ in Hindi, ‘Manthori khizangu’ in Malayalam, and ‘Kazhappai kizhangu’ in Tamil. The species has been domesticated more recently following its overexploitation in the natural habitats. Paracetamol is a common antipyretic agent, which is safe in therapeutic doses but can produce fatal hepatic necrosis in man, rats and mice with toxic doses. Protection against paracetamol – induced toxicity has been used as a test for potential hepatoprotective activity by several investigators. Based on the beneficial properties of Gloriosa superba tuber extract as a hepatoprotectant against paracetamol induced hepatotoxicity in experimental rats and delineate the mechanism of action by studying the alteration in enzymic activities and antioxidant status.

Materials and methods:

Collection of plant material:-

The tubers of Gloriosa superba were collected from ayurveda shop of Tharapuram district of Tamilnadu, India.

Preparation of Aqueous extract:-

The tubers were shade dried at room temperature and powdered, weighed 10gm of plant powder and dissolved in 100ml of distilled water and mixed well and the extract was filtered through Whatmann No. 1 filter paper. This extract was used for further analysis.

Preliminary Phytochemical analysis of aqueous extract of Gloriosa superb:-

Qualitative phytochemical analysis of aqueous extract of Gloriosa superba tubers was performed by the method of Peach and Tracy, 1955.

Animals used:-

The female Wistar strains albino rats weighing between 100-150 gm were obtained from Small Animal Breeding Center, Kerala Agricultural University, Trissur.
Experimental setup:-

Rats were divided into three groups comprising of six animals each.

Group I – Normal healthy rats were served as Control.

Group II – Administered paracetamol (200μg/kg/) orally for 2 days.

Group III – Received Gloriosa superba (500mg/kg/ bw /po) for 5 days followed by paracetamol (200 μg/kg/).orally for 2 days.

**Preparation of Tissue Homogenate:-**

At the end of experimental period, the animals were killed by cervical decapitation. Blood was collected, Serum separated and used for determination of biochemical constituents. Liver was removed and washed with ice-cold saline. A 10 % homogenate of the washed kidney tissues were prepared in 0.01 M Tris- HCL buffer, pH 7.4. The homogenate was centrifuged for 30min and the supernatant was used for the assay of enzymes.

**Assay of Enzymic and Non-Enzymic Antioxidants:-**

Enzymic antioxidants such as Catalase (Sinha, 1972.), Glutathione peroxidase (Rotruck et al., 1973), Non-Enzymic antioxidants such as Ascorbic acid (Omaye et al., 1979), Reduced Glutathione (GSH) (Moron et al., 1979) and Lipid Per oxidation (Uchiyama and Mahara, 1978) were measured.

**Results And Discussion:-**

I. **Preliminary phytochemical analysis of Gloriosa superba tubers:**

The phytochemicals present in Gloriosa superba tubers is presented in table. This shows that aqueous extract contains Alkaloids, Carbohydrates, Proteins, Thiols.
II. Assay of Enzymic and Non-enzymic antioxidants:-

1. Assay of Lipid per oxidation:-

Lipid per oxidation has been implicated in a number of pathological status. It can be use as a measure of oxidative damage. Peroxidation causes damage in the structure, fluidity and permeability of membrane, inactivates membrane bound enzymes and protein-receptors, induces swelling and alterations in respiratory functions, causes loss of –SH groups from membrane bound proteins, mediates DNA damage, carcinogenesis is also related to lipid peroxidation. The level of lipid per oxidation was significantly increased (p<0.01) in serum of Paracetamol treated Group II rats. After the treatment with plant extract the value showed near normal in group III rats, which proved the medicinal value of the plant. Thus from the above result it was evident that the activity of LPO was brought back to normal range on treatment with tuber extract in Paracetamol treated rats.

2. Assay of Reduced Glutathione (GSH) and Vitamin C:-

The levels of non-enzymic antioxidants, glutathione (GSH) and vitamin-C in control and experimental rats. The activity of reduced Glutathione enzyme and ascorbic acid were significantly decreased (p<0.01) in serum of Paracetamol treated hepatic damaged rats. After the treatment with plant extract the value showed near normal in group III rats, which proved the medicinal value of the plant. Thus from the above result it was evident that the activity of GSH&VIT C was brought back to normal range on treatment with tuber extract in Paracetamol treated rats.

3. Assay of Catalase and Glutathione Peroxidase (GPx):-

Catalase is found in both cytosol (70%) and mitochondria (30%) of various tissues. The activity of enzymes were significantly decreased (p<0.01) in serum of Paracetamol treated rats. After the treatment with plant extract the value showed near normal in group III rats, which proved the medicinal value of the plant. Thus from the above result it was evident that the activity of CAT &
GPx were brought back to normal range on treatment with tuber extract in Paracetamol treated rats.

Decreased activity of CAT and GPx were observed after the administration of Paracetamol to experimental rats, suggesting an increased concentration of peroxides, thereby a balance between the pro oxidant-antioxidant status is diminished.
3.3.3.6 Gloriosa superba L. (family Colchicaceae): Remedy or poison?

A. Maroyi1* and L. J. G. van der Maesen2,

1Biodiversity Department, School of Molecular and Life Sciences, University of Limpopo, Private Bag X1106, Sovenga 0727, South Africa.

2Netherlands Centre for Biodiversity Naturalis (Section National Herbarium of the Netherlands – Wageningen Branch), (Herbarium Vadense), Biosystematics Group, Wageningen University, Generaal Foulkesweg 37, 6703 BL Wageningen, The Netherlands.

Abstract:-

This article gives an overview of medicinal uses and poisonous properties of Gloriosa superba L., and the available literature related to these aspects drawn from studies done in areas where the species is utilized as traditional medicine or reported as poisonous. A list of 45 ethnobotanical applications practiced in 31 tropical African and Asian countries was drawn. A considerable convergence in ethnobotanical uses and practices emerged from these data. This comparative analysis strengthens the firm belief that ethnobotanical findings represent not only an important shared heritage, developed over the centuries, but also a considerable mass of data that should be exploited in order to provide new and useful knowledge of plant resources. Further ethnopharmacological studies are necessary to increase our understanding of the links between the documented traditional uses of G. superba, public health issues and its phytochemistry and pharmacological properties.

Key words:-- Colchicine, Gloriosa superba, poisonous, toxicity and traditional medicine.

Introduction:--

Gloriosa superba L. (family Colchicaceae) is not only a notorious human and livestock poison, but is also widely used in several indigenous systems of medicine for the treatment of various human
ailments. G. superba has caused illnesses and even fatalities to humans and animals due to both intentional and accidental poisoning. It is a native to tropical Africa, India and south-eastern Asia (Bunyapraphatsara and van Valkenburg, 1999), now widely cultivated throughout the world as an ornamental plant. G. superba is a tuberous plant with V or L-shaped, finger-like tubers that are pure white when young, becoming brown with age. It is a climbing herb, sometimes erect up to 6 m long, bearing pointed, dark green, glossy leaves, each equipped with a tendril by means of which it clings onto other plants. Leaves occur in whorls of 3 to 4, opposite or alternate, simple, sessile, ovate to lanceolate ranging from 6 to 20 cm in length and 1.5 to 4 cm wide. The attractive flowers are borne on long stalks and have six erect petals ranging in colour from bright yellow to bicoloured, red and yellow or purple and yellow. The fruits are capsules that split open to release several smooth red seeds with a spongy testa. It is common in forest-savanna boundaries, locally common in thickets, hedges, open forest, grassland and bush land, where it can be seen scrambling through other shrubs (Dounias, 2006). G. superba is commonly called Glory lily, flame lily, climbing lily, creeping lily in English; Lis de Malabar, lis grimpant, lis glorieux in French; Garras de tigre, aranha de emposse in Portuguese and Mkalamu, kimanja nouchawi in Swahili (Neuwinger, 1996). This review is aimed at compiling an up-to-date medicinal uses and poisonous properties of G. superba over its distributional range.

Review Procedure:-

The medicinal uses and poisonous properties of G. Superba were collated over its distributional range. Available references or reports on the species were consulted from published articles, books and book chapters, theses and abstracts available at international online databases such as web of science, scopus and google scholar and journals’ web sites. Suitable books or potential literature sources were identified in online databases of the particular libraries by searching for the terms
ethno medicine, traditional medicine, folk medicine, indigenous medicine, ethno botany and botanical medicine, poisonous properties, phytochemistry, pharmacological, toxicological properties of G. superba. References were also identified by searching the extensive library collections of the National Herbarium and Botanic Gardens, Harare, Zimbabwe; Wageningen, University, the Netherlands; University of Limpopo and Rhodes University, both in South Africa.

**Medicinal uses of G. superba:**

G. superba is a well-known non-wood forest product that has long been in regular demand amongst practitioners of traditional medicine in tropical African and Asian countries since antiquity. In India, it is a much used plant in Ayurvedic and Unani systems of medicines (Chopra et al., 1956; Watt, 1972); it is used either as a single drug or in combination with other drugs. Herbal medicine recommends G. superba for the treatment of urinary and reproductive systems, respiratory, skin diseases, cardiovascular troubles, and many other disorders. The seeds of G. superba are highly priced in the world market as sources of colchicine (Figure 1), a chemical that has been used in the past as a remedy against gout, a disease caused by deposits of uric acid in the joints (Sivakumar and Krishnamurthy, 2002). G. superba is used for treating a wide range of human ailments throughout the tropics. In India, the Ayurvedic Pharmacopoeia recommends G. superba as an ecbolic in labour, purgative, an anthelminthic and cure against leprosy, colics, chronic ulcers, haemorrhoids, skin parasites, head lice and tumours (Bunyaphraphatsara and van Valkenburg, 1999; Geetha et al., 2007; Jagtap et al., 2006; Jain et al., 2004; Katewa et al., 2004; Neuwinger, 1996; Sandhya et al., 2006; Satri, 1956; Tiwari and Yadav, 2003). The tuberous root stock of G. superba is boiled with Sesamum oil and applied twice a day on the joints as a remedy against arthritis and to reduce pain (Singh, 1993). The sap from the leaf tip is used as a smoothening agent for pimples and skin eruptions (Hemaiswarya et al., 2009). Seeds are used for relieving rheumatic pain and as a muscle
relaxant (Nadkarni, 2002). Traditionally, water extract of G. superba tuber has been used as an abortifacient (Burkill, 1995; Dounias, 2006; Ghani, 1998; Haerdi, 1964; Jain et al., 2004; Manandhar, 2002; Neuwinger, 1996; Sandhya et al., 2006), as a cure against venereal diseases (Dounias, 2006; Neuwinger, 1996; Yamanda, 1999), abdominal and general body pain (Dounias, 2006; Haerdi, 1964; Manandhar, 2002; Neuwinger, 1996). It is also used around doors and windows to repel snakes and also used as an antidote for snake bite and scorpion sting. Five different plant parts of G. superba are cited as important in ethnobotanical applications: leaves, seeds, unripe fruit, the root stock or tuber and the whole plant. The tuber or root stock is the plant part that is most frequently used (Dounias, 2006; Neuwinger, 1996). Five different pharmaceutical forms were cited, comprising paste, decoction (preparation in hot water), maceration (soaking in cold water), powder and using the whole plant without specific preparation. The decoction and the maceration are used for the majority of internal body ailments, like abdominal pain (Dounias, 2006; Haerdi, 1964; Manandhar, 2002; Neuwinger, 1996; Saralamp et al., 1996), coughs (Dounias, 2006; Haerdi, 1964; Neuwinger, 1996), fever and malaria (Ghani, 1998; Siddique et al., 2004), etc. Tuber paste of G. superba is applied externally to treat venereal diseases (Dounias, 2006; Neuwinger, 1996; Yamanda, 1999), wounds (Burkill, 1995; Dounias, 2006; Haerdi, 1964; Hassan and Roy, 2005; Katewa et al., 2004; Neuwinger, 1996), parasitic skin diseases (Dounias, 2006; Hassan and Roy, 2005; Watt and Breyer-Brandwijk, 1962) and head lice (Burkill, 1995; Haerdi, 1964; Maradjo, 1977; Neuwinger, 1996; Watt and Breyer-Brandwijk, 1962). G. superba is often used directly without any specific preparation around doors and windows to repel snakes and scorpions.
Poisonous properties of G. superba:-

G. superba is most commonly used as a remedy for skin diseases, as an abortifacient, snake bite or scorpion sting antidote, murder poison, suicidal agent and culpable homicide, head lice killer and as cure for wounds. The dominance of poisoning categories e.g. abortifacient, murder poisoning, head lice killer, treatment of skin diseases (antiparasitic) among the major uses of G. superba is not surprising. The toxicity effects of G. superba are well documented (Aleem, 1992; Bunyapraphatsara and van Valkenburg, 1999; Dasheiff and Ramirez, 1985; Jana and Shekhawat, 2011; Neuwinger, 1996; Reynolds and Oakley, 1984; Sechi et al., 2003; Van Wyk et al., 2002; Verdcourt and Trump, 1969; Watt and Breyer-Brandwijk, 1962; Wisniewski and Terry, 1967). The experimental use of colchicine on rats and monkeys has been shown to induce epileptic foci in rats, causing generalized seizures and death in both animals (Dasheiff and Ramirez, 1985; Reynolds and Oakley, 1984; Sechi et al., 2003; Wisniewski and Terry, 1967). Its applications in folk medicine over the years seem to exploit its poisonous constituents. (Bunyapraphatsara and van Valkenburg, 1999; Verdcourt and Trump, 1969).

Traditional healers seem to be aware of its toxicity as the amounts they prescribe to their patients are such that the toxic symptoms are minimized. Using larger dosages usually result in poisoning and death of the patients. Its poisonous properties are due mainly to colchicine (Figure 1), the tropolon alkaloid regarded as the biological hallmark of the family Colchicacae to which G. superba belongs (Hegnauer, 1963; Raffauf, 1970; Wildman and Pursey, 1968). Colchicine is documented as one of the seven upavishas (semi-poisonous drugs) in the Indian medicine, which cure many ailments but may prove fatal on misuse (Jana and Shekhawat, 2011; Joshi, 1993; Malpani et al., 2011). Other compounds such as colchicoside, gloriosine, lumicolchicine, 3-demethyl-N-deformyl-Ndeacetylcolchicine, 3-demethylcolchicine and N-formyl deacetylcolchicine
have also been isolated from the plant (Ade and Rai, 2009; Suri et al., 2001). A new colchicine, glycoside, 3-O-demethylcolchicine-3-O-alpha-Dglucopyranoside from G. superba seeds has recently been described (Suri et al., 2001). The use of tubers and seeds of G. superba in traditional medicine have caused numerous human deaths in tropical Africa (Van Wyk et al., 2002; Verdcourt and Trump, 1969; Watt and Breyer-Brandwijk, 1962), India and Sri Lanka (Aleem, 1992; Eddleston, 2000; Fernando, 2001; Fernando and Fernando, 1990). G. superba has also been used for centuries for homicide, suicide and inducing abortion (Eddleston, 2000; Modi, 1988; Saravanapavanathan, 1985). In Nigeria, G. superba tuber is added to conventional arrow poisons, for example, Strophanthus sarmentosus DC. and S. hispidus DC. (Neuwinger, 1996). Both intentional and accidental poisoning with G. superba has been reported from Africa and Asia (Agunawella and Fernando, 1971; Dunuwille et al., 1968; Eddleston, 2000; Watt and Breyer-Brandwijk, 1962). The tubers of G. superba have been documented as dangerous to grazing stock in tropical Africa, causing stock losses in some instances (Burkill, 1995; Dalziel, 1955; Neuwinger, 1996; Watt and Breyer-Brandwijk, 1962) and it is used in some cases to poison cattle particularly in India (Satri, 1956).

Other activities:

Other studies have evaluated the enzyme inhibition activities of G. superba rhizome extract against lipoxygenase, acetylcholinesterase, butyrycholinesterase and urease in which wonderful inhibition was observed on lipoxygenase (Khan et al., 2007). The aqueous extract of G. superba root showed oxytocic activity and early abortifacient activity on the female reproductive system of rat (Malpani et al., 2011). These findings provide justification for the use of G. superba as an abortifacient and other ethnobotanical uses as shown in Table.
Conclusions:-

The pharmacological studies conducted on G. superba indicate the immense potential of this plant species in the treatment of inflammatory, parasitic and bacterial ailments. Different pharmacological studies in a number of experiments have convincingly demonstrated the ability of G. superba to exhibit a wide range of pharmacological activities lending support to the rationale behind several of its traditional ethnobotanical uses as detailed in Table. These results may justify the use of G. superba as an anti-inflammatory and anti-microbial medicine in a couple of African and Asian countries.

Toxicity and adverse effects:-

10 mg of colchicine has been documented as the toxic dose which may cause a lethal effect in humans (Rigante et al., 2006). According to this research, colchicine is not associated with reduced fertility rate in women or with a higher miscarriage rate and stillbirths; on the contrary colchicine might improve female fertility and pregnancy outcome. An observation that contradicts the findings of Malpani et al. (2011), who found colchicine to have oxytocic activity and early abortifacient activity on the reproductive system of female rats. More than 40 mg of colchicine in humans is invariably fatal within three days of ingestion (Bruneton, 1999). Side effects associated with its use as a cure for FMF are listed. Side effects increases in older patients or in those affected by liver or kidney failure (Rigante et al., 2006). Just after ingestion of toxic levels of colchicine, the symptoms develop within two hours. The first signs of toxicity include vomiting, numbness and severe effects on throat as well as diarrhea leading to dehydration. Alopecia and dermatitis are the major symptoms that develop after two to three weeks after poisoning (Cerquaglia et al., 2005; Maxwell et al., 2002; Rigante et al., 2006). Multi-organ failure can develop 24 to 72 h after ingestion. These
include bone marrow depression, hemolytic anemia, liver damage, renal failure, respiratory distress syndrome, arrhythmias, neuromuscular disturbances, paralysis and disseminated intravascular coagulation (Cerquaglia et al., 2005; Maxwell et al., 2002; Rigante et al., 2006). Over dosage may frequently lead to a cholera-like syndrome associated with dehydration, shock, acute renal failure, alopecia, hyperthermia, hepatocellular failure, epileptic seizures, coma and death (Rigante et al., 2006). Correlation between the ethnomedicinal employment and the pharmacological activities has been duly observed and described in the present review. Of particular promise due to its cytotoxic activity against a number of cancer cells is the colchicine alkaloid and related compounds. In fact, these findings suggest that G. superba has the potential to be developed as a chemotherapeutic agent to prevent or to inhibit the growth of tumours and cancers. While there are still gaps in the studies conducted so far, which need to be bridged in order to exploit the full medicinal potential of G. superba, it is still very clear that this widespread plant species has tremendous potential for the future. There is need for further research, clinical trials and product development. However, there is a need to study the acute toxicity, sub-acute toxicity, chronic toxicity and pharmacological safety associated with the use of G. superba as medicine. Detailed animal and human acute and chronic toxicity studies of colchicine and its derivatives are required prior to clinical testing. Traditional healers seem to be aware of its toxicity as the amounts they prescribe are such that toxic symptoms are minimized. Using larger dosages usually result in poisoning human. On the basis of current information and evidence, G. superba extracts are characterized by instances of toxicity and it should be used under supervision of a physician.
3.2.4 Tagetes Erecta

3.2.4.1 Combined Wound Healing Activity Of Tagetes Erecta Linn :

Kiranmai M, Kazim SM and Ibrahim M*

Department of Pharmacology and Biotechnology, Nizam Institute of Pharmacy, Deshmukhi, Pochampally (Mandal), Near Ramoji Film City, Nalgonda 508284, Andhra Pradesh & Asian Institute of Advance Research, Hyderabad 500058, Andhra Pradesh, India.

Abstract:-

To screen the wound healing activity of carbopol gels prepared from hydro alcoholic extracts of Gymnema sylvestere (GE) and Tagetes erecta Linn. (TE) in excision wound model and burn wound models in albino mice. Formulations of the extracts was done in the form of gels of carbopol individually and also in combination in equal ratio. In excision and burn wound models, the so treated animals showed significant reduction in period of epithelization and wound contraction and combined gel showed accelerated wound healing activity may be because of synergism. The enhanced wound healing activity of hydro alcoholic extracts may be due to free radical scavenging action and the phytoconstituents (flavonoids) present in it which either due to their individual or additive effect fastens the process of wound healing. Presence of flavonoids in alcoholic extracts was confirmed by phytochemical investigation and TLC methods.

Keywords: Gymnema sylvestere and Tagetes erecta Linn., wound healing activity and hydro alcoholic extract

Introduction:-A wound is a disruption of tissue integrity that results in damage and is typically associated with loss of function. Wound healing can be defined as a complex dynamic process that results in the restoration of anatomic continuity and function. Healing of wounds usually takes
place in a direction away from its normal course and under healing, over healing or no healing of wounds is common. Management of under healing of wounds is a complicated and expensive programme and research on drugs that increase wound healing is a developing area in modern biomedical science. Many ayurvedic medicinal plants have a very important role in process of wound healing. Plants are more potent healers because they promote the repair mechanisms in the natural way. The healing process can be physically monitored by assessing the rate of contraction of the wound. 3 Gymnema sylvestre (Asclepiadaceae) is native to central and western India. It is a potent antidiabetic plant used in folk, ayurvedic and homeopathic systems of medicine. It is used in the treatment of asthma, eye complaints, inflammation and snake bite. It possesses antimicrobial, anti-inflammatory, antihyperlipidemic, hepatoprotective and sweet suppression properties. 4, 5 GE leaves contain triterpene saponinsoleanane and dammarene classes, oleanane saponins are gymnemic acids and gymnema saponins, while dammarene saponins are gymnemasides. 6 Tagetes erecta Linn. (Asteraceae) commonly known as marigold is a common garden plant. The leaves are reported to be effective against piles, kidney troubles, muscular pain, ulcers, and wounds. The pounded leaves are used as an external application to boils and carbuncles. It is reported to have antioxidant, antimycotic, analgesic activity and 18 active compounds are identified by GC-MS, many of them are Terpenoids. 8-10 Both the plants especially leaves are having good wound healing activity individually. 11 The present study has been undertaken to ascertain the combined wound healing effect of carbopol gels of GE and TE leaves on experimentally induced wounds in mice.

Materials And Methods:-

Plant material:-

Leaves of Gymnema sylvestre and Tagetes erecta Linn were collected from local areas of Hyderabad
shade dried and were authenticated from botany department, Osmania University, Hyderabad.

**Preparation of extracts:-**

100g of leaves of both the plants were powdered to coarse form. The powdered materials were loaded in soxhlet extractor and defatted with petroleum ether (40-60°C). The marc was dried and extracted with ethanol (50 % v/v) in a same extractor up to three cycles. Finally the extracts were concentrated to semi solid mass using rotary evaporator under vacuum. The traces of solvent were removed by keeping the dried extract in to a desiccator. Gymnema sylvestre extract was labeled as GSE and Tagetes erecta Linn extract was labeled as TEE.

**Phytochemical studies:-**

The individual extracts were subjected to qualitative chemical investigation for the identification of the phytoconstituents: sterols, alkaloids, glycosides, saponins, carbohydrates, flavonoids and tannins.

**Thin Layer Chromatography (TLC):** was performed for both the extracts by using suitable solvent system. Mobile phase for GEE is n-butanol-water-methanol (10:10:1) and for TEE is ethyl acetate: formic acid: glacial acetic acid: water (100: 11: 11: 26). Pre coated silica gel is acted as stationary phase in both the experiments.

**Experimental :-**

**Animals:** Healthy adult albino mice weighing between 25-40 g were procured from the institute. The animals were caged individually after wounding for treatment till completion of wound healing. In each group of different models six animals were used. The experimental protocol was approved by institutional animal ethics committee and animals were maintained under standard conditions in an animal house approved by committee for the purpose of control and supervision on an experiment on animals (CPCSEA).
Chemical :-

Metrozyl gel was procured from hetero pharmacy (Hyderabad) and carbopol, methyl paraben and propyl paraben were procured from SD fine chemicals Pvt. Ltd. (Mumbai).

Toxicity Studies:-

Toxicity studies of alcoholic extract were carried out in oral doses of 100 to 2000 mg/kg- body weight using albino mice. After test extract administration, animals were observed 72 hr. period. The numbered of deaths was expressed as a percentile and the LD50 was determined by probate a test using the death percentage versus the log dose. Study protocol was approved from the Institutional Animal Ethics Committee (IAEC).

Evaluation of Wound Healing Activity:-

Excision model:-

Randomly collected mice of both sex, weighing between 25-40 g. Divided them into five groups of six in each and are placed in different cages. Treatment groups: Group I: carbopol gel, Group II: GSE gel, Group III: TEE gel, Group IV: CE gel, Group V: Standard (metrozyl gel) For the excision wound study each group containing six animals was selected. A circular wound of about 10mm diameter was made on depilated dorsal thoracic region of mice under light ether anesthesia in aseptic condition and observed throughout the study. Animals were housed individually. Group-I animals are applied with 2.5% of carbopol gel. Group II & III are applied with 2.5% of GSE and TEE gels respectively. Group IV is applied with 2.5% of CE as thin layer twice daily. Group V animals are applied with metrozyl gel twice daily as thin layer. Wound area can be measured on 2,4,6,8,10,12,14,16,18,20,22nd post wounding days. % of wound contraction was calculated from the day of measurement of wound area and epithelization period was also calculated.
**Burn wound model:-**

Wax is heated to a temperature above 1000c and is poured as a drop on the mice skin to create a wound on the dorsal thoracic region 1cm away from the vertebral column and 5cm away from the ear. Area of the wound was measured in sqmm by placing a transparent polythene graph over the wound and then traced the area of the wound on it. This is taken as initial wound area reading.

Group-I animals are applied with 2.5% of carbopol gel. Group II & III are applied with 2.5% of GSE and TEE gels respectively. Group IV is applied with 2.5% of CE as thin layer twice daily. Group V animals are applied with metrozyl gel twice daily as thin layer. Wound area can be measured on 2,4,6,8,10,12,14,16,18,20,22nd post wounding day. % of wound contraction was calculated from the day of measurement of wound area and epithelization period was also calculated.

**Conclusion :-**

The present study has demonstrated that hydro alcholoc extract of Gymnema sylvestre, Tagetes erecta and their combined extract have properties that render it capable of promoting accelerated wound healing activity compared with placebo controls. Wound contraction, qualitative tests and TLC support further evaluation of synergistic wound healing effect of these two plants and even stability studies of their carbopol gels in the topical treatment and management of wounds.
3.2.4.2 Formulation and in vitro evaluation for sun protection factor of Lutein ester extracted from Tagetes erecta Linn flower (Family-Asteraceae) sunscreen creams:-


Abstract:-

The effectiveness of Sunscreens is determined by sun protection factors (SPF), which is supposed to indicate the level of protection from UV radiation. The present study was designed to study the sunscreen activity of herbal formulation containing lutein ester extracted from Tagetes erecta L. flowers (Family Asteraceae). This study investigates its in vitro sun protection factor (SPF) by COLIPA method of Lutein ester in a cream formulation. The Sun Protection Factor of lutein ester cream exhibited less activity (SPF= 1.08±0.02) with Boot Star Rating 4 which approaches to good sunscreen activity. The described in vitro method, though, presents some limits; it has spared the exposure of human subjects to harmful ultraviolet radiations that can pose potential risks of skin cancer, hence, it is still preferred and is undoubtedly beneficial as it gives accurate and reproducible results. This method has thus helped to determine the SPF value of a novel drug like Tagetes erecta L. (Asteraceae) and stating that it has good sunscreen activity and can be considered as active sunscreen agent or can be incorporated into other sunscreen formulations as an additive to enhance the activity.

Key words: lutein ester, Tagetes erecta, sunscreen, Sun Protection Factor, Boot Star Rating.
3.2.4.3 A Concise Review on Tagetes Erecta:-

G. Gopi1, A. Elumalai2 and P. Jayasri3
1Department of Pharmaceutics, Mahathi College of Pharmacy, CTM X Road, Chittoor (Dt), Madanapalle, Andhra Pradesh, 517 319.
2Department of Pharmacognosy, Anurag Pharmacy College, Ananthagiri (V), Kodad (M), Nalgonda (Dt), Andhra Pradesh, 508 206.
3Department of Pharmacognosy, Santhiram College of Pharmacy, Srinivas Nagar, Kurnool (Dt), Nandyal, Andhra Pradesh, 518 501.

Abstract:-

Medicinal plants have been of great importance to the health care needs of individuals and their communities. The use of herbal preparations made from medicinal plants is widespread in developing countries. The healing powers of traditional herbal medicines have been realized since antiquities. About 65% of the world populations have access to local medicinal plant knowledge system. India is sitting on a gold mine of well-recorded and traditionally well practiced knowledge of herbal medicine. This article discusses about the medicinal values of Tagetes erecta. In this communication, we reviewed the pharmacological and phytochemistry of Tagetes erecta and its application in the treatment of various ailments like the flower parts of plants are used as a hepatoprotective, insecticide, anti-oxidants and analgesic. This review discusses the investigation made by various workers related to chemical constituents, pharmacological action and toxicological studies of this plant since years till date.

Key words:
Tagetes erecta, Pharmacological Actions, Toxicological Studies.

Introduction:-

Medicinal plants and derived medicine are widely used in traditional cultures all over the world and they are becoming increasingly popular in modern society as natural alternatives to synthetic
chemicals. In the last few decades there has been an exponential growth in the field of herbal medicine. It is getting popularized in developing and developed countries owing to its natural origin and lesser side effects. At the present juncture, the modern conventional healthcare is burdened with great problems of unsafe medicines, chronic diseases, resistant infections, autoimmune disorders and degenerative disorders of ageing, despite great scientific advances. More than 70% of India’s 1.1 billion populations still use these non-allopathic systems of medicine. India possesses almost 8% of the estimated biodiversity of the world with around 0.126% million species. The World Health Organization (WHO) estimated that approximately 80% of world population relies mainly on traditional medicines, mostly plant drugs in their health care. Today, Ayurveda coexists with modern system of medicine, and is still widely used and practiced. About 30% of the currently used therapeutics is of natural origin.

**Pharmacological Actions:-**

**Anti-bacterial Activity :-**

Rhma and Madhavan reported the anti-bacterial activity of different solvents of Tagetes erecta flowers against *Alcaligens faecalis*, *Bacillus cereus*, *Campylobacter coli*, *Escherchia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Proteus vulgaris*, *Streptococcus mutans* and *Streptococcus pyogenes*. The flavonoid possesses anti-bacterial activity against all the tested strains and shows maximum zone of inhibition for *Klebsiella pneumoniae* (29.50 mm). The flavonoid-Patulitrin is one of the potential elements for its anti-bacterial activity.

**Antimicrobial Activity:-**

Ruddock et al reported the anti microbial activity in 19 plants used in Colombian traditional medicine for cutaneous infections, were screened against *Neisseria gonorrhoeae* (NG) by disc susceptibility assay. In all, 71% of the crude extracts exhibited antibacterial activity against the
antibiotic susceptible NG strain, whereas 10% of the extracts inhibited penicillinase-producing NG strain GC1–182. The Tagetes erecta flower parts showed maximum inhibitory action against NG strain.

**Anti-oxidant activity:-**

Chivde et al reported the antioxidant studies on the ethanolic extract of Tagetes erecta flowers by three different assays like DPPH, reducing power and super oxide radical scavenging activity at different concentrations were used. In all the three assay, Tagetes erecta showed better reducing power than the standard (i.e. ascorbic acid), and super oxide anion scavenging activity and DPPH antioxidant activity showed less than standard. However, ethanolic extract of Tagetes erecta demonstrated antioxidant property in all the in Vitro models.

**Hepatoprotective activity:-**

Bose et al reported the hepatoprotective activity in flowers of Tagetes erecta by carbon tetra chloride induced hepatopathy model. The ethanolic extract showed the increase in serum ALT, AST, ALP and bilirubin levels. Ethyl acetate fraction of T. erecta (EATE) at the dose of 400 mg/kg orally significantly decreased the elevated serum marker enzymes and level of bilirubin almost to the normal level compared to CCl4-intoxicated group. Histological changes in the liver of rats treated with 400 mg/kg of EATE extract and CCl4 showed a significant recovery except cytoplasmic vascular degenerations around portal tracts, mild inflammation and foci of lobular inflammation. Phytoconstituents such as flavonoids, terpenoids and steroids are responsible for the observed hepatoprotective activity.

**Insecticidal activity:-**

Nikkon et al reported the insecticidal activity in Tagetes erecta flowers against a stored product insect pest, Tribolium castaneum (Herbst). The chloroform fraction showed highest toxicity against
both the larvae and adults of Tribolium castaneum followed by petroleum ether fraction and ethanol extract. The LC values of chloroform fraction against first, second, third, fourth, fifth and sixth instar larvae were 11.64, 14.23, 19.26, 29.02, 36.66, 59.51 μg/cm² (72 h.), respectively and for adults the value was 65.93 μg/cm² (72 h.). No mortality was observed in control. Finally they concluded that the flower of Tagetes erecta might be a pesticide against Tribolium castaneum.

Mosquitocidal activity Nikkon et al reported the mosquitocidal activity in ethanolic, chloroform and petroleum ether extracts of Tagetes erecta flowers against different instars of Cx.quinquefasciatus. Among the tested samples the chloroform soluble fractions showed the highest toxicity and consequently the LC50 values (14.14μg/mL, 17.06μg/mL, 36.88μg/mL and 75.48μg/mL) for all instar larvae of Cx.quinquefasciatus. The larvae showed comparative tolerance in the course of increasing age and time. From this they concluded the flowers of Tagetes erecta having good mosquitocidal activity.

**Nematicidal activity:**

Husain et al reported the nematicidal efficacy of four medicinal plants viz. Azadirachta indica, Calotropis procera, Datura stramonium and Tagetes erecta was ascertained for the control of M. incognita. All leaf amendments at different dosages significantly improved the plant growth characteristics of okra and reduced root-knot infections compared with the untreated control.

**Wound healing activity:**

Ibrahim et al reported the wound healing activity of carbopol gels prepared from hydro alcoholic extracts of Gymnema sylvestere (GE) and Tagetes erecta Linn. (TE) in excision wound model and burn wound models in albino mice. In excision and burn wound models, the GE and TE treated animals showed significant reduction in period of epithelization and wound contraction and combined gel showed accelerated wound healing activity may be because of synergism. The
enhanced wound healing activity of hydro alcoholic extracts may be due to free radical scavenging action and the phytoconstituents (flavonoids) present in it which either due to their individual or additive effect fastens the process of wound healing.

**Larvicidal activity:**

Marques et al reported the larvicidal activity of essential oil from Tagetes erecta against 3rd instars of Aedes aegypti and to determine the amounts of larvicidal thiophenes in all plant tissues. The oil obtained by steam distillation and analyzed by gas chromatography/mass spectrometry showed 14 compounds. The main compounds were piperitone (45.72%), d-limonene (9.67%), and piperitenone (5.89%). The essential oil was active against larvae of Aedes aegypti, with LC50 of 79.78 μg/ml and LC90 of 100.84μg/ml. The larvicidal thiophene contents were higher in the roots and flowers as demonstrated by high-performance liquid chromatography analysis. Thus, Tagetes erecta constitutes a good source of varied compounds showing larvicidal activity against Aedes aegypti.

**Sub acute toxicity studies:**

Nikkon et al reported the sub acute toxicity studies in chloroform fraction from ethanol extract of Tagetes erecta flower by solvent-solvent partitioning method. The sub acute toxicity of chloroform fraction was evaluated on Long Evan’s rats at 200 and 400 mg/kg doses and the results obtained from chloroform fraction treated rats were compared with untreated controls. Treatment of chloroform fraction at 200 and 400 mg/kg doses did not make any significant alterations on the hematological and biochemical parameters of rats when data were compared with that of untreated controls. Histopathological examination also showed no detectable changes in liver, kidney, heart and lung of chloroform fraction treated rats. This study revealed that the chloroform fraction of Tagetes erecta had no toxic effects.
Conclusion:-

The extensive literature survey revealed that Tagetes erecta is important medicinal plant with diverse pharmacological spectrum. The plant shows the presence of many chemical constituents which are responsible for varied pharmacological and medicinal property. The evaluation needs to be carried out on Tagetes erecta in order to uses and formulation of the plant in their practical clinical applications, which can be used for the welfare of the mankind.

3.2.4.4 Antinociceptive and Anti-Inflammatory Effects of Solvent Extracts of Tagetes erecta Linn (Asteraceae):-

NV Shinde*, KG Kanase, VC Shilimkar, VR Undale and AV Bhosale, SGRS College of Pharmacy, Department of Pharmacology, Pune University, Saswad, Tal-Purandar, Pune 412301, India

Abstract:-

Purpose:-

Traditionally, the leaves of Tagetes erecta L. are used in India for the alleviation of pain and inflammation. The objective of this study was to investigate the antinociceptive and anti-inflammatory activities of this plant material in an animal model.

Methods:-

The chloroform, methanol and ether extracts of the leaves of Tagetes erecta L. (family: Asteraceae) were tested against acetic acid-induced writhing in mice and carrageenan-induced paw oedema in rats in order to assess their antinociceptive and anti-inflammatory activities, respectively. The doses administered intraperitoneally (I.P.) ranged from 100 to 400 mg/kg body weight, and acetylsalicylic acid (ASA) and phenylbutazone were the reference standards for the antinociceptive and anti-inflammatory tests, respectively.
Results:

The extracts showed antinociceptive and anti-inflammatory properties at doses between 200-400 mg/kg. They inhibited significantly (P < 0.005), in a dose-dependent manner, induced writhing reflexes in mice. The antinociceptive effect was comparable to that of ASA which served as the reference standard. Similarly, the extracts significantly (P < 0.05) reduced carragenan-induced paw oedema in rats and the reduction in paw volume was comparable to that of the reference standard (phenylbutazone). It also increased pain threshold in the oedematous right hind limb paw of the rats.

Conclusion:

The results obtained show that the extracts of Tagetes erecta L. (Asteraceae) has antinociceptive and anti-inflammatory properties. This finding provides a basis for the traditional use of the plant material.

Keywords:

Tagetes erecta, Antinociceptive, Anti-inflammatory.
3.2.4.5: Photoprotective Effects of Hydroalcohol Tagetes Erecta Extract Against UV-Induced Oxidative Damage in Mice:

Monika Sachdeva1*, Murli Dhar Kharya2, Ahmed Aljarbou3 and Taruna Katyal4

1College of Pharmacy, Qassim University, Buraidah, Saudi Arabia,
2Department of Pharmaceutical Sciences, Dr. H.S Gour University, Sagar, M.P., India,
3College of Pharmacy, Qassim University, Buraidah, Saudi Arabia,
4I.S.F. College of Pharmacy, Moga, Panjab, India.

Abstract:

Purpose: To investigate the effects of topical application of Tagetes erecta hydroalcohol extract as a dermal antioxidant agent and evaluate its capacity to prevent ultraviolet (UV)–induced oxidative damage.

Methods: The plant flower was extracted with aqueous ethanol (60%). Female Lacca mice were divided into five groups of 24 animals each. Group I was un-irradiated control (neither UV exposure nor any treatment received). Group II was irradiated control and received 5 min UV exposure twice a day. Groups III, IV and V received both UV exposure and treatment of different concentrations of the extract, 4 h. prior to UV exposure. The degree of protection was quantified using biochemical tests (lipid peroxidation and glutathione level) and histopathological assessment.

Results: The results showed that 2% topical extract treatment reduced the effect of UV light-induced photoaging on mice skin by decreasing malondialdehyde (MDA) level by up to 50% and increasing glutathione (GSH) level 3-fold (p < 0.01) compared to UV-irradiated control group. Histopathological evaluation also indicated a photo-protective effect on the extract-treated mice skin as no signs of histological changes were seen after UV exposure.
Conclusion: -

Topical application of T. erecta has a potential for preventing oxidative damage by UV irradiation.

Keywords:-

T. erecta, Photo-ageing, skin wrinkles, Antioxidants, Oxidative damage, UV radiation.
3.2.4.6: Supercritical CO$_2$ extraction of oleoresin from marigold (*Tagetes erecta* L.) flowers and determination of its antioxidant components with online HPLC-ABTS•+ assay:

Gong, Y., Plander, S., Xu, H., Simandi, B. and Gao, Y. (2011),

College of Food Science and Nutritional Engineering, China Agricultural University, Beijing 100083, China

Department of Chemical and Environmental Process Engineering, Budapest University of Technology and Economics, H-1521 Budapest, Hungary

**Abstract:**

**Background:** Marigold is a traditional medicine herb which shows good pharmacological activity in many aspects. It is very important to obtain and investigate the specific bioactive compounds from marigold. The objective of the study was to extract the oleoresin from marigold with supercritical CO$_2$ (SC-CO$_2$) at different pressures and temperatures, detect the fatty acid composition by gas chromatography–mass spectrometry and investigate the antioxidative components in the extracts by combined online high-performance liquid chromatography-2,2-azinobis-(3-ethylbenzothiazolin-6-sulfonic acid (HPLC-ABTS•+) post-column assay and HPLC-tandem mass spectrometry.

**Results:** For the pressure range (20–40 MPa) and temperature range (30–70 °C), 30 MPa/70 °C gave the highest yield of oleoresin (58.9 g kg$^{-1}$). The dominant fatty acids of marigold flower oleoresin were linoleic acid (>26.41%), palmitic acid (>24.22%) and oleinic acid (>20.12%). Significant effects of the extraction pressure and temperature on the antioxidant activity were observed ($P < 0.05$). Lutein esters, α-tocopherol, β-tocopherol, γ-tocopherol and δ-tocopherol were the dominant antioxidant compounds in the extracts.
Conclusion:

The study has shown that the yield and total antioxidant activity of the marigold extracts were affected by the pressure and temperature of SC-CO$_2$, and that online HPLC technique could be used as an efficient and rapid method for separation and identification of bioactive compounds from a complex mixture.

Keywords:

Marigold; supercritical carbon dioxide; antioxidant activity; online HPLC-ABTS$^{++}$; HPLC-MS/MS.
3.2.4.7 Systematic review of herbals as potential anti-inflammatory agents: Recent advances, current clinical status and future perspectives:-

Sarwar Beg1, Suryakanta Swain2, Hameed Hasan3, M Abul Barkat3, Md Sarfaraz Hussain4

1 Department of Pharmaceutics, Faculty of Pharmacy, Jamia Hamdard, Hamdard Nagar, New Delhi, India (2011)

2 Department of Pharmaceutics, Roland Institute of Pharmaceutical Sciences, Khodasingi, Berhampur, Orissa, India (2011)

3 Department of Pharmacognosy, Faculty of Pharmacy, Jamia Hamdard, Hamdard Nagar, New Delhi, India (2011)

4 Department of Pharmacognosy, Faculty of Pharmacy, Integral University, Khursi Road, Lucknow, India (2011)

Abstract:-

Many synthetic drugs reported to be used for the treatment of inflammatory disorders are of least interest now a days due to their potential side effects and serious adverse effects and as they are found to be highly unsafe for human assistance. Since the last few decades, herbal drugs have regained their popularity in treatment against several human ailments. Herbals containing anti-inflammatory activity (AIA) are topics of immense interest due to the absence of several problems in them, which are associated with synthetic preparations. The primary objective of this review is to provide a deep overview of the recently explored anti-inflammatory agents belonging to various classes of phytocconstituents like alkaloids, glycosides, terpenoids, steroids, polyphenolic compounds, and also the compounds isolated from plants of marine origin, algae and fungi. Also, it enlists a distended view on potential interactions between herbals and synthetic preparations, related adverse effects and clinical trials done on herbals for exploring their AIA. The basic aim of
this review is to give updated knowledge regarding plants which will be valuable for the scientists working in the field of anti-inflammatory natural chemistry.

**Keywords:**

Alkaloids, anti-inflammatory agents, cannabinoids, clinical trials, glycosides, herbals, inflammation
3.2.4.7 Investigation into the antioxidant activity and chemical composition of alcoholic extracts from defatted marigold (Tagetes erecta L.) residue:

Ying Gong, Xuan Liu, Wen-Hao He, Hong-Gao Xu, Fang Yuan, Yan-Xiang Gao (2011)

College of Food Science & Nutritional Engineering, China Agricultural University, Beijing, China

Abstract:

The influence of various solvents on the yield of polyphenols from defatted marigold residue, the antioxidant activity of the extracts and the composition of antioxidant compounds in the extracts were investigated. The content of total phenolics and flavonoids in the extracts was significantly varied with different solvents (P < 0.05) and the extract by ethyl alcohol (EtOH)/water (7:3, v/v) has the highest content of total phenolics and flavonoids, 62.33 mg gallic acid equivalents (GAE)/g and 97.00 mg rutin equivalent (RE)/g, respectively. The antioxidant activity of the extracts was evaluated by radical (2,2′-azino-bis-(3-ethylbenzothiazoline-6-sulfonic acid) (ABTS), 1,1-diphenyl-2-picrylhydrazyl (DPPH)) scavenging and ferric reducing antioxidant power (FRAP) assays. The results of the correlation analysis showed that the antioxidant activity was well correlated with the content of total phenolics and flavonoids (R² > 0.900). Antioxidant components in the extracts were identified by combined on-line HPLC–ABTS, post-column assay and HPLC–DAD–MS method. Gallic acid, gallicin, quercetagetin, 6-hydroxykaempferol-O-hexoside, patuletin-O-hexoside and quercetin were the dominant antioxidant compounds in the extracts, and quercetagetin was identified as the strongest antioxidant capacity.