Original Article

Preparation And Standardization Of A Polyherbal Formulation For Analgesic Activity Of Selected Plants

Upendra Singh[1] , Dr. Shikhar Verma[2]

[1]Research Scholar, Maharishi School of Pharmaceutical Science, MUIT, Lucknow.
[2]Professor, Maharishi School of Pharmaceutical Science, MUIT, Lucknow.
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Abstract

Ayurveda is the oldest healing system of medicine. Major formulations used in Ayurveda are based on herbs. The medicinal herbs are used as decoctions, infusions, tinctures, and powders. Ayurvedic treaties like Charaka, Sushruta have included special chapters on Ayurvedic preparations in the chapters on "Kalp-Sthana". It deals with methods of preparation and dose of formulations. When two or more herbs are used in formulations, they are known as polyherbal formulations. Some time herbs are also combined with mineral preparations. The concept of polyherbalism is peculiar to Ayurveda although it is difficult to explain in terms of modern parameters. Sanghar "samhita" highlights the concept of synergism behind polyherbal formulations. Thus the present study aimed to preparation and standardization of a polyherbal formulation for analgesic activity. The present research work concluded that three selected herbs; Syzygium cumini leaves, Moringa oleifera leaves and stem of Cissus quadrangularis showed significant ($p<0.05$) analgesic activities in their methanolic & aqueous extracts.

KEYWORDS: Syzygium cumini leaves, Moringa oleifera leaves and stem of Cissus quadrangularis, analgesic activity & polyherbal formulation.

INTRODUCTION

Substances produced from natural resources have been used for avariety of reasons, including management of pain, since the dawn of time. Opium, for example, has been used from beginning of time, around 7000 years ago. Natural products, on other hand, have dominated drug business for manyyears, & numerous marketed medications arebased on isolates from them. Natural product research has recently seen a renaissance, particularly in dietary supplement business. The pharmaceutical business has begunto reinvigorate natural product screening procedures. Initially, research in field ofpain treatment & drug addiction concentrated solely on natural products. Analogs derived from natural chemicals have lately been released onto the market, as have wholly synthesized compounds based on natural pharmacophores. The science and medical disciplines are still grappling with the unfavorable side-effect profiles of these analgesic compounds. Naturaproducts are still being explored for novel chemical structures that mayinteract with established analgesic targets, in addition to rational drug design and wholly unique synthetic initiatives. The pharmacology of pain has become a complicated area, with more potential pharmacological targets being uncovered as more systems methods are examined. This review will highlight some of most recent studies of new, naturally derivedanalgesia chemicals.

PAIN MECHANISMSAND CONTROL

Pain can be described as any unpleasant physical or emotional experience. The most prevalent cause for seeking medical treatment is pain. There are 2 sorts of pain: acute pain and chronic pain. Acute pain acts as a warning mechanism to avoid certain pain sources. Chronic pain can exist at any moment and for any reason, and it appears to serve no obvious function. Chronic pain treatment is a big issue owing to the usage of current drugs & their negative side-effect qualities. The side effects of today's pain drugs vary depending on kind of agent employed; nonetheless, most medical experts are concerned with addiction, tolerance, gastrointestinal symptoms, and

misuse. Recentclinical studies indicate that effective pain therapy has a minimal risk of developing addicts, & as a result, prescribing efforts appear to be changing [1].

Endogenous inflammation pain-producing chemicals, it should be noted, can operate synergistically to raise pain levels. Nociceptors (or pain receptors) are located not just in the skin but also in other parts of the body. As previously stated, brain & spinal cord play a significant part in central pain processes. However, our understanding of brain pathways remains inadequate. Among the neurotransmitters and receptors found in dorsal horn of spinal cord are substance P, a substance called neuropeptide Y, excitatory amino acids, inhibiting amino acids, nitric oxide, naturally occurring opioids, adenosine, & monoamines. It is obvious that pain propagation to brain is subject to a variety of physiological controls.

ASPIRIN

Aspirin (acetylsalicylicacid) is made from salicylic acid, which is extracted from bark of Willow tree (Salix alba). Aspirin was first nonsteroidalanti-inflammatory drug (NSAID), & it works by blocking arachidonic acidpathway, which results in production of eicosanoids,which are powerful pain mediators [2].

Aspirin, which inhibits cyclooxygenase (COX) enzymes in particular, cleared the door for the creation of more synthetic nonsteroidalanti-inflammatory drugs (NSAIDs). Indeed, study into the COX system's molecular cascade resulted in the creation of COX-2 enzyme inhibitors, which were previously commended for having safer profilesthan other NSAIDS(which block COX-1 enzyme).

OPIOIDS

Opioid is the generic term for any chemicals with same mechanismof action as opium components. All opioids interact with endogenous opioidreceptor system, which is made up of four receptor subtypes [3]: mu, delta, kappa, & ORL-1 (opioid receptorlike receptor). These receptors are found in all vertebrates & are widely distributed throughout mammalian system. The investigation of opioid systems has focused on 3 types of modulators. Natural chemicals such as morphine, codeine, & thebaine fall within first group. The second & third are not included in this review, however they are synthetic compounds that were created utilizing knowledge of natural product pharmaceuticals & peptides, respectively.

Salvinorin A, first non-nitrogenousselective kappa opioid receptor ligand described by Roth BL et al [4], has lately received a lot of study interest. Salvinorin A, the primary ingredient in Salvia divinorium preparations, is one of most powerful hallucinogens known to date (Gautam V, 2003). Salvinorin A was first tested against a battery of receptors, none of which were opioid receptors [5].

Due to psychotropic nature of kappa opioid receptor system, this made logical sense. Because of the dysphoric side-effects they induce, kappa opioid receptor agonists have not found favor as analgesic medicines. Salvinorin A has been shown to causedysphoric hallucinations in the majority of human volunteers (Siebert DJ, 1994). However, the United States Drug EnforcementAgency continues to designate itas a chemical of concern since it is now promoted as a legal alternative toother illicit hallucinogens. Salvia divinorium extracts are easily available on the Internet, and only a few jurisdictions restrict sales to individuals above the age of 18.

Salvinorin A's unusual structure suggests that it isinteracting in anovel manner with kappa opioid receptor & may serve as a viable lead chemical for creation of novel opioid receptor ligands. In this context, our study has focused on salvinorin A's possible analgesic qualities, with the objective of understanding manner of interaction with kappa opioid receptors & perhaps developing a helpful ligand from these investigations. Salvinorin an is a highly selective template for the synthesis of kappa opioid receptor antagonists, which is of tremendous interest in the pharmaceutical sector.

Although salvinorinA is most researched & well-characterized nonnitrogenous kappa opioidreceptor agonist at this time, it is notonly non-nitrogenous chemical identified to interact with opioid receptors.Pawhuskin A, a stilbene derivative derived from Dalea purpurea, was recently revealed to exhibit minimal affinity foropioid receptors [6].

Native Americans utilized this herb to fight against sickness and treat nonspecific diseases. Because organic extracts of this plant displayed mild opioid action, components in this extract were isolated. Pawhuskin A displayed the greatest opioid receptor affinity of any isolated molecule from D. purpurea to date, with a 290 nM affinity. Although the researchers conducted receptor binding studies using a non-selective1radioligand, it is uncertain which opioid receptor(s) are responsible for activity. Furthermore, no functional activity for

pawhuskin A has beenreported, therefore it has to be determined if it is an agonist of the opioid receptor & whether it may genuinely serve as alead chemical for development of novelanalgesics based on the the stilbene in order scaffold.

Analgesic effects have been observed for extracts of Dicleagrandiflora, a vine found in NortheasternBrazil [7]. Several non-nitrogenous chemicals were identified from these extracts, & a small component, dioflorin, was found tobe a powerful analgesic ina tail-flick mouse model [8]. Naloxone reversed the analgesic effect, indicating a possible way of interaction with opioid receptors. However, no receptor bindingdata have been published to yet, & it is still unknown ifthis chemical produces antinociception preferentially by direct contact with opioid receptors.

Menthol, extracted from peppermint (Mentha piperita), has been used for millennia as an antipruritic, antimicrobial, and cooling in topical treatments. It interacts with and activates cold receptors [9]. It was recently tested in hot-plate & acetic acid abdominal constriction experiments, where it showed substantial action [10].

Furthermore, naloxone & kappa opioid receptor selective antagonist, norBNI, abolished the effects, indicating an interaction with opioid receptors, & more specifically, kappa opioid receptors. It was discovered thatmenthol has no effect on motor activity. However, no opioidreceptor binding data has been published. Given importance of opioid receptors & their interaction with ion channels, where menthol is knownto operate, a more complicated suppression of opioid receptor signaling pathways may be implicated. More research is needed regardless of particular mechanism of action.

As additional chemicalcomponents of traditionally usedplants for pain relief are identified, thereis significant potential for creation of innovative opioid receptor-based pharmacological therapies.

VOLTAGE-GATED ION CHANNELS

It has been discovered that several natural compounds interact with voltage-gated ion channels. Cocaine extracted from Erythroxylon coca is perhaps most well-known ligand that inhibits sodiumchannels [11]. Cocaine is most recognized & studied for itsability to inhibit dopamine transporter in order to induce euphoria [12]. However, its use as a local anesthetic is recognized due to itsinteractions via sodium channel blocking.

Tetrodotoxin, which was discovered frompuffer fish, inhibits sodium channels & causes severe injury to humans who consume it. Within 20 minutes of intake, it causes numbness in the lips and tongue, but it swiftly progresses to paralysis and, in rare circumstances, death. In Japan, where puffer fish liverdish, fugu, is a delicacy, this is a serious worry. The hazardous nature of this molecule has restricted its usage as a lead chemical for analgesic research.

Batrachotoxin, which was discovered from poison dart frogPhyllobates terribilis, was found to activate sodium channels[13]. It is clear that frog doesnot generate this chemical, & it is thought to be derived from adietary insectsource. This toxinis very toxic, with a fatal dosage in humans estimated to be between 2 and 200 mg [14]. Brevetoxins havebeen linked to redtide (a vast natural bloom ofalgae in saltwater) & have been blamed for enormous fish fatalities. Brevetoxin Bhas been produced & has been shown to bind to sodiumchannels [15].

Brevetoxins, once again, are chemicals thatcan aid researchers in understanding pharmacology and toxicity of sodium channelactivation,but they are unlikely to function as possible analgesic chemicals.

Calcium channels have also been implicated in pain pathways [16]. When potassium channels are activated, the membrane becomes hyperpolarized, which reduces cellexcitability. Depending on where thesechannels are located, theymay either operate in a direct or indirect manner in the transmission of pain signals. Severalanesthetics used in clinical practice now interact with potassiumchannels [17]. Certainpeptides derived from naturalsources have also been discovered.

Calcium channels have been extensively researched fortheir role in smooth muscle contraction [18]. Calcium channel blockers, in particular, have shown to be effective in treatment ofhypertension on the prescription medicine market. Calcium channels, on the other hand, are appealing targets for analgesia & neurological protection. They appear to have the ability to either inhibitor increase opioid action. L-type calciumchannels may inhibit opioid tolerance [19], & clinical studies with thesedrugs should yield intriguing findings.

Conus spp. have demonstrated to be a significant source of novel peptides with a wide range of pharmacological actions [20]. Cone snails hunt by injecting their prey with venom containing a wide variety of identical peptides, eventually paralyzing theirprey for ingestion. One of these peptides, N-conotoxin, hasbeen

identifiedto interact with N-type calciumchannels. This medication hasbeen demonstrated to be 100-1000 timesmore potent than morphine inanalgesia studies while being non-addictive [21], making N-typecalcium channels intriguing targets for development of newanalgesics.

ACETYLCHOLINE RECEPTORS

Themuscarinic acetylcholinereceptors & nicotinic acetylcholine receptorsare the 2 types of acetylcholinereceptors. These classeswere discovered through use of natural compounds such as muscarine & nicotine. These receptors have a well-documented involvement in regulation ofcentral nociception; nevertheless, therapeutic success has yet to be achieved.

Natural product ligands for muscarinic acetylcholine receptors include hyoscyamine,atropine, scopolamine & & Mamba snake poisons. These havebeen thoroughly covered in literature & will not be discussed further here.

The receptors for nicotine acetylcholinehave been shown to have a more important function inanalgesia. Nicotine was initially identified as an antinociceptive in [22]. Until discovery of naturally occurring alkaloidepibatidine [23], this field of inquiry was mostly unknown. Epibatidine, produced from skin of Ecuadorian dart-frog Epipedobatestricolor, was shown to be a potentanalgesic compound thatcould be suppressed by the nicotinic receptor antagonist mecamylamine but not byopioid antagonists. This work showed importance of the nicotinic receptors for acetyl in analgesia & piqued the attention of researchers in developing novel epibatidine-related medicines.

CANNABINOID RECEPTORS

Cannabinoid receptors are another well-known system implicated in nociceptive processes. D9-tetrahydrocannabinol, derived from Cannabis sativa, is a non-nitrogenous lipophilic compound that binds to cannabinoid G-protein coupled receptors [24]. This was very certainly first nonnitrogenous ligand known to interact with a GPCR. In the United States, it is now marketed for treatment of nausea & vomiting associated with cancer chemotherapy, as well as as an appetite stimulant for individuals suffering from AIDS wasting disorder [25]. It has also been proven in people and animals to cause antinociception (Grotenhermen F, 2004).

The anandamides are endogenous families of ligandsthat bind withthese receptors. They are lipids that were found lately. Anandamide is antinociceptive on its own, although not as strong as THC [26]. It has been discovered that the enzyme fatty acid amides the hydrolase (FAAH) rapidly degrades it [27]. Endogenous anandamide, which levels in FAAH knockout mice were shown to be 15 times greater than inwild-type mice [28]. Furthermore, in nociception models, these animals appear to have a larger pain threshold. This study shows that targeting FAAH enzymes for antinociceptive therapy has promise. As cannabinoid system research advances, it is quite likely that aligand will enter market as a novel technique to treat pain.

VANILLOIDRECEPTORS

Many in the commercial and academic research communities have recently focused on vanilloid receptors (VR) as a possible targetfor novel analgesics. Vanilloid receptors are ion channels that have been linked to sensory processes. Their clinical potential, however, has yet to be demonstrated. Nonetheless, some natural compounds have been discovered as receptor modulators.

Capsaicin, a VR1 receptor agonist derived from redhot chili peppers,is commercialized in United States intopical formulations for treatment of arthritis & inflammatory jointpain [29]. These treatments have downsides in that they might cause significant irritationto mucous membranes & eyes. They do, however, have a profitable market, which leads researchersto conclude thatVR1 receptor agonists might be promising pharmaceutical options. Anothernatural substance that hasbeen found as a VR1 receptoragonist is resiniferatoxin, which is extracted from succulent plant Euphorbiaresinifera [30]. Several studies inliterature show resiniferatoxin's use as an analgesic drug. Recently, Karai et colleagues [31] shown that resiniferatoxin treatment preferentially ablates nociceptive neurons. As a result, the prospect of developing drugs that interact with VR1 receptors remains intriguing.

Mushrooms have also been shown to have naturally occurring chemicals that act on VR1 receptors. The molecule, a triprenylphenol, belongs to a new structural family of vanilloidreceptor ligands. Isovelleral is a fungal metabolite ofpungent mushrooms that contains anunsaturated 1, 4-dialdehyde molecule & belongs to a different

chemical class. It has been proven that these chemicals generate irritating effects by activating capsaicin-sensitive vanilloid receptors [32].
The various methods to screen analgesics using different pain stimuli are summarized below

TABALE 1 SCREENING METHODS FOR ANALGESIC AGENTS [33]

PAIN STIMULUS	SPECIES	METHODS
Thermal Method	Mouse/Rat	Hot plate method
	Mouse/Rat	Tail flick test
	Mouse/Rat	Tail immersion test
	Mouse/Rat	Radiant heat method using analgesiomete
Mechanical Methods	Mouse/Rat	Tail pressure
	Any	Skin pressure
	Any	Distension of hallow viscera
Chemical Methods	Mouse/Rat	Writhing test or peritoneal irritation method
Electrical Stimulation	Dog, Rabbit, Guinea Pig	Tooth pulp stimulation
	Mouse	Pododolorimeter

OBJECTIVES OF STUDY

The main objectives of present study are:

1. To study the importance of traditional medicines and polyherbal formulations.
2. To develop herbal medicines for analgesic activity.
3. Screening for analgesic activity

RESEARCH METHODOLOGY

In present study, fresh leaves of Syzygium cumini Linn, leaves of Moringa oleifera Lam. and fresh stems of Cissusquadrangularis Linn. werecollected, from Botanical garden of Kim College of pharmacy respectively, Gujarat. The plants were identified bycomparing it morphological & microscopical characterswith description given indifferent standard texts & floras.

Soon after authentification, all leaves and stems weredried atroom temperature, untilthey were free from moisture & subjected to physicalevaluation with different parameters. The parameters, which were used for evaluation, are nature, odour,colour, taste, size, shape, width, and length. Finally leaves and stems were subjected to size reduction to get coarse powder and then passed through sieve no.40 toget uniform powder. Then the uniformpowder was subjected to standardization with different parameters as per Pharmacopoeias/ literature.

SCREENING FOR ANALGESIC ACTIVITY

ANIMAL SELECTION

The experiment used albino rats ofeither sexes weighing 150 to200 grams. They were used to test analgesic activity. Ratswere placed into eight groups of six rats each. Every day, bedding materials in the cages was replaced.

MATERIALS

Extract used:

- Methanolic extract of Syzygium cumini

- Aqueousextract of Syzygium cumini
- Methanolicextract of Moringaoleifera
- Aqueous extract ofMoringa oleifera
- Methanolic extractof Cissus quadrangularis
- Aqueous extract of Cissus quadrangularis
- Standard: Pentazocin. (FORTWIN, Ranbaxy, India)

DOSE SELECTION

- Methanolic extract of Syzygium cumini. (300 mg/kgb.wt)
- Aqueous extract of Syzygium cumini. (300 mg/kgb.wt)
- Methanolic extract of Moringa oleifera. (600 mg/kgb.wt)
- Aqueous extractof Moringa oleifera. (600 mg/kgb.wt)
- Methanolicextract of Cissus quadrangularis. (300 mg/kgb.wt)
- Aqueous extract of Cissus quadrangularis. (300 mg/kgb.wt)
- Control: five mL/kg of five percent gum acacia. (p.o.)
- Standard: Pentazocin five mg/kg bodyweight (i.p.)

METHOD

The analgesicresponses of givensamples ofextracts were evaluated using tail immersion method To assess analgesic activity, ratswere separated into eight groups(each group including 6 animals) using Chandrashekar technique. The first groupwas servedas the control & got just five percent acacia solution (5mL/kg bdwt,orally), while second groupwas provided as the norm & received the standard medicine Pentazocin (five mg/kg bd wt, i.p.). Theremaining animal groupswere given various extracts of Syzygium cumini, Moringa oleifera, and Cissus quadrangularis. The tail immersion method was used to assess analgesic reactions of plant extracts. The albino rats were weighed and marked throughout this operation. They areplaced in individual restraining cages, with tail free to dangle. Before testing, the animals are given 30 minutes to adjust to their new surroundings. The lower five cm of the tail is indicated. This part of tail is immersed in acup offreshly filled water ofexactly 55±5ºC. Within a few a few seconds, rat withdraws its tail. The animals were given standard, test, & control dosages, and their response times were recorded at 0, 30, 60, 90, 120, 150, and 180 minutes.

RESULTS AND DISCUSSION

A variety of approaches for assessing analgesic efficacy in animals have been devised using the concepts of thermal, mechanical, chemical, or electrical stimuli. The most often used way of assessing analgesic activity is a change in reaction time of an animal subjected to a heat stimulation, such as tail immersion or tail flick test. It is known thatseveral chemicalmediators, i.e., bradykinin and prostaglandin, produces pain in thermalinjury and that μ, δ, & κ opiodreceptor agonists mediatepotent antinociceptive activity in animals subjected to thermalinjury. Since pentazocine exhibits high affinity for μ1, μ2 and κ1 opioid receptor, it is proposed that pantazocine may exhibits antinociception against thermal stimulus via thesereceptors. In present study, individual treatment with pentazocine and different alcoholic and aqueous extract of the various plants part demonstrate significant analgesic activity over the standard (Tables 2, 3, 4 and Figures 1, 2, 3).

TABLE 2: ANALGESICACTIVITY OF VARIOUSEXTRACTS OF LEAVES OF SYZYGIUM CUMINI

Sl. No	Groups(n)	0min	30min	60min	90min	120 min	180 min
		MEAN ± SD					
1	Control	2.69 ± 0.05	2.87 ± 0.04	2.90 ± 0.03	2.91 ± 0.03	2.89 ± 0.06	2.80 ± 0.03
2	Standard	2.95	3.05	4.50	5.32	5.01	4.22

		± 0.03	± 0.04	± 0.03	± 0.04	± 0.05	± 0.02
3	Methanol extract of SC	2.57 ± 0.02	3.48 ± 0.03	4.24 ± 0.02	5.01 ± 0.03	4.75 ± 0.03	4.70 ± 0.03
4	Aqueous extract of SC	2.89 ± 0.02	2.97 ± 0.02	4.49 ± 0.03	5.20 ± 0.03	4.75 ± 0.03	4.41 ± 0.04

* = Significant, ** = highlysignificant. (p <0.05), N= 6,

From results obtained it is concludedthat an aqueous extract (2.89 ± 0.02) of Syzygium cumini (ASCE) and methanolic extract (2.57 ± 0.02) of Syzygium cumini (MSCE) leaves show amoderate analgesic activity, while after 90min an aqueous extract (5.20** ± 0.03) of Syzygium cumini shows a highly significant activitywhile in case of methanolic extract (5.01* ± 0.03) of Syzygium cumini shows a moderately significant analgesic activitywhen compared to standarddrug (5.32** ± 0.04).

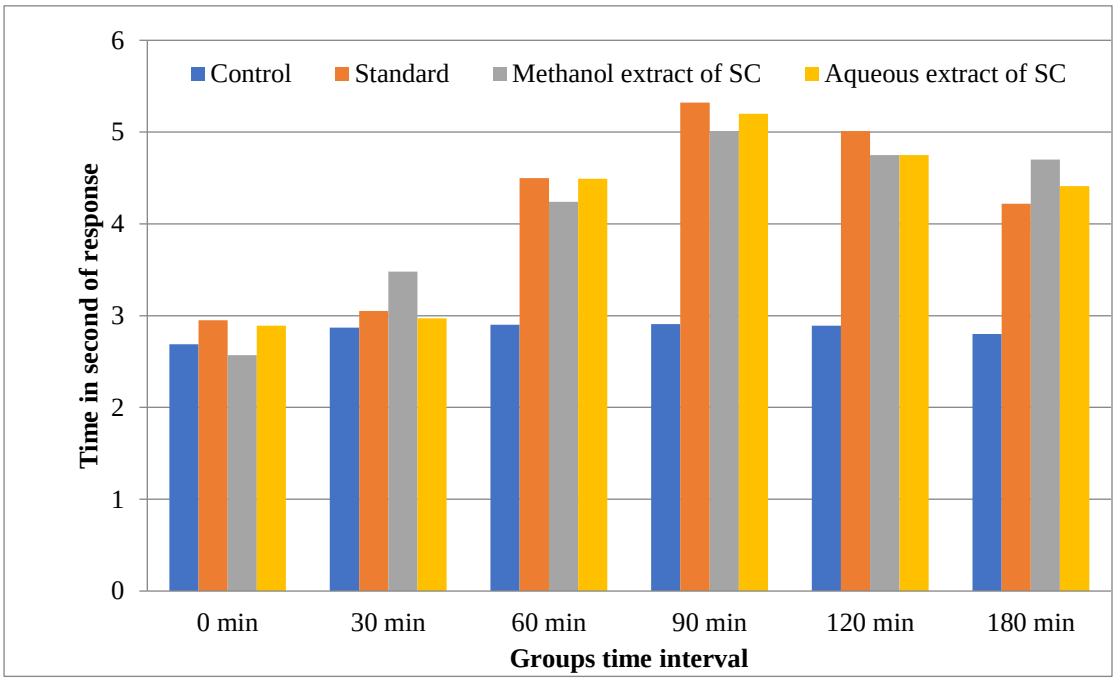

FIGURE 1: ANALGESIC ACTIVITYOF VARIOUS EXTRACTS OF LEAVES OF SYZYGIUM CUMINI

TABLE 3: ANALGESIC ACTIVITY OFVARIOUS EXTRACTSOF LEAVES OF MORINGA OLEIFERA

Sl. No	Groups (n)	0min	30min	60min	90min	120 min	180 min
		MEAN ± SD					
1	Control	2.69 ± 0.05	2.87 ± 0.04	2.90 ± 0.03	2.91 ± 0.03	2.89 ± 0.06	2.80 ± 0.03
2	Standard	2.95 ± 0.03	3.05 ± 0.04	4.50 ± 0.03	5.32 ± 0.04	5.01 ± 0.05	4.22 ± 0.02
3	Methanol extract of MO	2.60 ± 0.03	3.51 ± 0.03	4.28 ± 0.02	5.10 ± 0.03	4.82 ± 0.04	4.45 ± 0.02

4	Aqueous extract of MO	2.92 ± 0.02	3.01 ± 0.01	4.45 ± 0.03	5.18 ± 0.04	4.73 ± 0.0	4.45 ± 0.04

* = Significant, ** = highlysignificant. ($p<0.05$), n = 6,

From results obtained it is concluded thataqueous extract (2.92 ± 0.02) of Moringa oleifera (AMOE) and methanolic extract (2.60 ± 0.03) of Moringa oleifera (MMOE) showsmoderate analgesic activity, while after 90min aqueousextract (5.18** ± 0.04) of Moringa oleifera shows highly significant activitywhile in case of methanolicextract (5.10* ± 0.03) of Moringa oleifera shows moderate analgesic activity when compared to standard drug (5.32** ± 0.04).

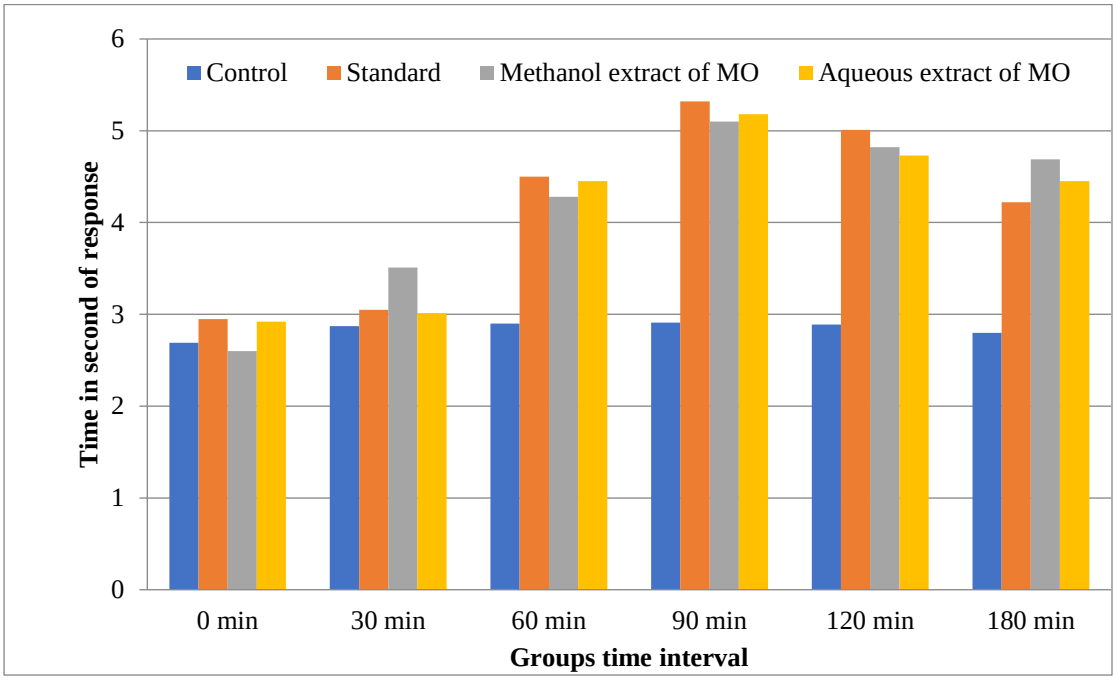

FIGURE 2: ANALGESIC ACTIVITY OFVARIOUS EXTRACTSOF LEAVESOF MORINGA OLEIFERA

TABLE 4: ANALGESIC ACTIVITY OF VARIOUSEXTRACTS OF STEM OF CISSUSQUADRANGULARIS

Sl. No	Groups (n)	0min	30min	60min	90min	120min	180min
		MEAN ± SD					
1	Control	2.69 ± 0.05	2.87 ± 0.04	2.90 ± 0.03	2.91 ± 0.03	2.89 ± 0.06	2.80 ± 0.03
2	Standard	2.95 ± 0.03	3.05 ± 0.04	4.50 ± 0.03	5.32 ± 0.04	5.01 ± 0.05	4.22 ± 0.02
3	Methanol extract of CQ	2.70 ± 0.03	3.61 ± 0.03	4.38 ± 0.04	5.22 ± 0.03	4.90 ± 0.02	4.73 ± 0.02
4	Aqueous extract of CQ	3.10 ± 0.03	3.20 ± 0.03	4.50 ± 0.03	5.22 ± 0.04	4.80 ± 0.04	4.62 ± 0.03

* = Significant, ** = highlysignificant. ($p<0.05$), n = 6,

From results obtained it is concluded thatmethanolic extract (2.70* ± 0.03) of Cissus quadrangularis (MCQE) shows moderate analgesic activity while aqueous extract (3.10* ± 0.03) of Cissus quadrangularis (ACQE)

showssignificant analgesic activity after90 min. While at 180 min both aqueousextract (4.62** ± 0.03) and methanolic extract (4.73** ± 0.02) of Cissus quadrangularis shows significant analgesic activitywhen compared to standarddrug (4.22** ± 0.02).

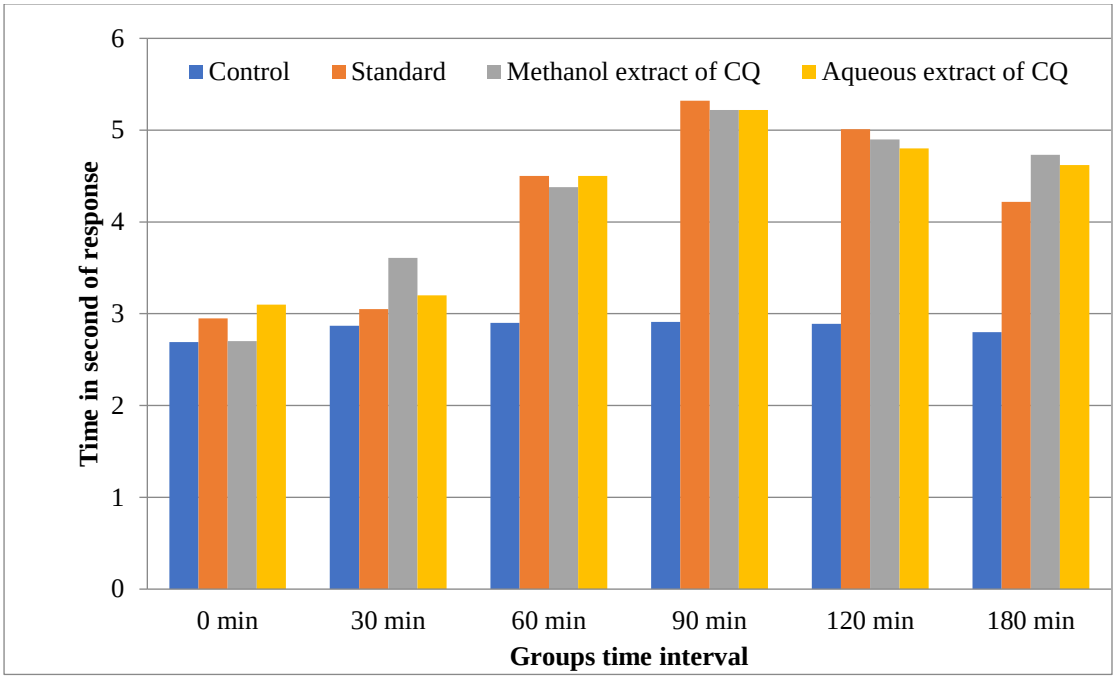

FIGURE 3: ANALGESIC ACTIVITY OF VARIOUS EXTRACTS OFSTEM OF CISSUSQUADRANGULARIS

CONCLUSION

At 180 min an aqueous extract (4.41** ± 0.04) of Syzygium cumini showsa highly significantactivity while in case of methanolicextract (4.70* ± 0.03) of Syzygium cumini it shows a moderately significant analgesic activitywhen compared to standarddrug (4.22** ± 0.02), while at 180 min aqueous extract (4.45** ± 0.04) of Moringa oleifera shows highly significant activity while in case of methanolic extract (4.69* ± 0.02) of Moringa oleifera shows moderate analgesic activity, at 180 min both aqueous extract (4.62** ± 0.03) and methanolic extract (4.73** ± 0.02) of Cissus quadrangularis shows significant analgesic activity when compared to standard drug (4.22** ± 0.02), ($p<0.05$). The present research work concluded that three selected herbs; Syzygium cumini leaves, Moringa oleifera leaves and stem of Cissus quadrangularis showed significant ($p<0.05$) analgesic activities in their methanolic & aqueous extracts.

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