MÆDICA - a Journal of Clinical Medicine

ORIGINAL PAPER

MAEDICA – a Journal of Clinical Medicine
2021; 16(1): 54-63
https://doi.org/10.26574/maedica.2021.16.1.54

MyrliMax® and Low Back Pain: A Multicentric, Observational, Post-Marketing Surveillance Study in Indian Patients Suffering from Chronic Low Back Pain of Various Pain Intensity

Varun SUREJA[a]*, Dharmeshkumar KHENI[a], Divyanshu PRAJAPATI[a], Mayank RAJAWAT[a], Ajit MAGAR[a], Asha KRISHNARAJ[a], Ashish SIRSIKAR[b], A ARUN PRASATH[c], Amit MISHRA[d], Anil Singh RAJPUT[e], Balasubramanian VIJAYAKRISHNAN[f], Chetan PURAM[g], D MANOJ KUMAR[h], Diwakar AGARWAL[i], Girish SHIRAGAMBHI[j], Jitendra PATIL[k], K RAVICHANDRAN[l], Kailash Nath JAIN[m], M THAYAGA RAJU[n], Rajesh ARORA[o], S NAWAZISH[p], Sachin CHHABRA[q], Lakshminarayan SHYAM[r], Sudarshan IS[s], Vinay AGGARWAL[t]

[a]Department of Medical Affairs, Sundyota Numandis Group of Companies, Ahmedabad, India

[b]Department of Orthopedics, N.S.C.B Medical College, Jabalpur, India

[c]Department of Orthopedics, APJ Multi-Speciality Hospital, Walajabad, India

[d]Department of Orthopedics, Suchak Hospital, Mumbai, India

[e]Department of Orthopedics, Rajput Fracture, Joint & Trauma Clinic, Gwalior, India

[f]Department of Orthopedics, Lifespan Bone & Joint Clinic, Chennai, India

[g]Department of Orthopedics, Sancheti Instituite for Orthopaedic & Rehabilitation, Pune, India

[h]Department of Orthopedics, Shri Kanaka Mahalaxmi Nursing Home, Vizag, India

[i]Department of Orthopedics, Diwakar Ortho & General Hospital, Jaipur, India

[j]Department of Orthopedics, Primus Hospital, Bengaluru, India

[k]Department of Orthopedics, Adarsh Nursing Home, Mumbai, India

Address for correspondence:
Varun SUREJA
Department of Medical Affairs, Sundyota Numandis Group of Companies,
7th Floor, 705-708 Tower A, Safal Pegasus, Prahalad Nagar, Ahmedabad-380015, Gujarat, India
Mobile: +91 7878016065
Email: varun@sundyotanumandis.com

Article received on the 28th of December 2020 and accepted for publication on the 26th of February 2021

[l]Deparment of Orthopedics, Jayam Hospital, Madurai, India

[m]Department of Orthopedics, Dr. Jain's Clinic, Delhi, India

[n]Department of Orthopedics, Radhika Clinic, Bengaluru, India

[o]Department of Orthopedics, Newlife Clinic, Delhi, India

[p]Department of Orthopedics, Nuha Hospital, Guntur, India

[q]Department of Orthopedics, Pusp Clinic, Indore, India

[r]Department of Orthopedics, Raksha Hospital, Madurai, India

[s]Department of Orthopedics, Bhargav Orthopedic Center & Banashankari Orthopedic Speciality Service, Bengaluru, India

[t]Department of Orthopedics, Sanjeevani Hospital, Delhi, India

ABSTRACT

Background: *Chronic low back pain (LBP) is the most common musculoskeletal condition affecting a person's quality of life. Over the past decades, a lot of work was done in an attempt to reduce the negative impact of LBP, and help patients recover and maintain a better quality of life. Nevertheless, there is still a lot to be done to fully understand the problem of underlying chronic LBP and a wide gap that exist between basic science and applied rehabilitation research on LBP.*

Objectives: *This was an open label, multicentric, observational, post-marketing surveillance study in a real-world setup designed to evaluate the efficacy and safety of MyrliMax® capsules containing standardised Commiphora myrrha gum resin extract in Indian subjects with chronic LBP varying in intensity.*

Material and methods: *This study included 204 subjects diagnosed with chronic LBP at the outpatient department of 20 centres under the supervision of a medical doctor. All subjects took MyrliMax® capsules twice daily for 20 days. Visual Analogue Scale (VAS) pain score, rescue medicine requirement, therapy satisfaction scores and safety parameters were assessed as per the schedule.*

Outcomes: *Treatment with MyrliMax® capsules significantly ($p<0.01$) and progressively reduced the VAS score throughout treatment. A significant pain reduction was observed from the second visit. The mean VAS score was 6.58, 4.66, 2.99 and 1.88 on Day 0, Day 7, Day 14 and Day 20, respectively. A similar trend was also observed in subgroups based on gender and severity score. The need of rescue analgesics/NSAIDs was significantly reduced from the second week, indicating a potential of MyrliMax® capsules to increase the pain threshold. All physicians and patients were satisfied with the efficacy of MyrliMax® capsules assessed by physician's satisfaction score and patient's satisfaction score. There were no significant serious adverse events due to treatment during the study, which indicated that the treatment with MyrliMax® was well tolerated by subjects.*

Conclusion: *MyrliMax® capsule is a potentially effective and safe therapy for pain reduction in patients suffering from chronic LBP. MyrliMax® capsules can be used to reduce pain in NSAIDs intolerant subjects suffering from chronic LBP.*

Keywords: MyrliMax®, *Commiphora myrrha* extract, chronic low back pain, furanodienes, analgesic.

INTRODUCTION

Chronic pain afflicts almost two billion people around the world (1). Low back pain (LBP) is defined as pain in the area of the posterior aspect of the body, from the lower margin of the 12th rib to the lower gluteal fold, that can relate to problems with the lumbar spine, discs between the vertebrae, ligaments around the spine and vertebral discs, spinal cord and nerves, muscles of the low back, internal organs of the pelvis and abdomen, or skin covering the lumbar area (2-4). Recurrent or chronic LBP (*i.e.*, LBP persisting for 12 weeks or more) is a common problem, with an enormous individual, economic and societal burden (5, 6). Patients with LBP experience intense radiating leg pain that may be accompanied by neurological signs, associated with high healthcare costs, work absenteeism, and economic burden (7). Most of times, the optimal treatment is based on targeting the underlying mechanisms of pain and tailoring the management modality for each patient using a personalized approach (8); however, nonsteroidal anti-inflammatory drugs at the lowest effective dose with few recommendations on the use of combination drug therapy are also used (9).

However, long-term administration of non-steroidal anti-inflammatory drugs (NSAIDs) may lead to numerous complications, such as stomach ulcers, liver failure, and cardiovascular toxicity and many other adverse effects, including nausea, constipation, and the risk of dependency (10, 11).

The gum resin extracts of *Commiphora myrrha* (Myrrh, syn. *C. molmol*) have been used since ancient times in traditional medicine in Europe (Romans and Greeks), Arabia, China and India, and myrrh was a common analgesic used to clean wounds and sores for more than 2000 years, until the discovery of morphine in Europe (12). Curzerene, furanoeudesma-1,3-diene and lindestrene are the main sesquiterpenes characterizing the chemical composition of *C. myrrha*, which show analgesic effects blocked by naloxone, indicating an interaction with brain opioid mechanisms (13). Recently, a powder extract of myrrh with a standardized content of these bioactive furanodienes was used in a pilot study in which a balanced sample of 95 female and 89 male volunteers was assessed to evaluate the analgesic effect of *C. myrrha* extract on different pain pathologies, including headache, fever-dependent pain, joint pain, muscle aches, low back pain and menstrual cramps (14).

Based on the consolidated efficacy of myrrh extract, we decided to focus on a new dietary supplement, MyrliMax® capsule, which is characterized by the presence of at least 4 mg of bioactive furanodienes from *C. myrrha* extracts. The aim of the study was to evaluate the efficacy and tolerability of *C. myrrha* extract (as MyrliMax® capsule) in outpatient subjects suffering from chronic LBP. ❑

MATERIAL AND METHODS

Study material

The nutraceutical composition was provided as MyrliMax® capsules (Sundyota Numandis Pharmaceuticals Pvt. Ltd., Ahmedabad, India). Each delayed release gastro-protectant hydroxypropyl methylcellulose capsule contained 100 mg of *C. myrrha* powder extract (corresponding to at least 4 mg of bioactive furanodienes), along with other excipients, including microcrystalline cellulose, magnesium stearate, talc and silicone dioxide.

Reagents and content of capsules

A standardized myrrh (*C. myrrha* Nees Engl.) powder extract, was provided by Biosfered S.r.l. (Turin, Italy) as a yellowish powder produced from myrrh gum resins with a total furanodienes content > 40 mg/g. Sigma-Aldrich (USA) provided the pure standard of trans-nerolidol, which was used as internal standard and dissolved in hexane (Sigma-Aldrich, USA) at a final concentration of 10 mg/mL. Aliquots of the stock solutions were stored in 1.5 mL HPLC vials at -80°C until use. The chemical purity and integrity of the standard compound were assessed prior to use.

Identification of *Commiphora myrrha* extract furanodienes

One hundred milligrams of a *C. myrrha* powder extract were added in a glass tube with 5 mL of acetone:hexane in ratio of 1:1 (VWR International, Radnor, PA, USA) (extraction ratio 1:50 w /v) and 500 µg of internal standard (*trans*-nerolidol).

The samples were vigorously mixed by vortexing, and the powder was then extracted in an ultrasonic bath at 30°C for 30 min. At the end of the extraction, the samples were mixed by vortexing and centrifuged for 10 min at 5,000 g. The supernatant of the solvent was collected in a glass tube. Extraction was repeated twice, and the solvent aliquots were combined in the same glass tube, as previously described (14).

Prior to analysis, the extracts were loaded into Pasteur pipettes filled with $MgSO_4$ (Fluka, USA) to filter the samples and remove any traces of water. The samples were then analyzed by gas chromatography (GC) coupled to mass spectrometry (MS) for qualitative analysis of the compounds and by GC coupled to a flame ionization detector (FID) for quantitative analysis. The GC-MS analyses were performed using an Agilent Technologies 6890N gas chromatograph coupled with an Agilent Technologies 5973A mass spectrometer using a Zebron ZB-5MS (Phenomenex, USA) capillary column (30 m length, 250 µm internal diameter, 0.25 µm film thickness). The injector temperature was set at 250°C, and a constant helium flow (1.0 mL min^{-1}) was used as the mobile phase. The following temperature program was used: initial temperature 50°C, followed by a linear thermal gradient of 3°C min^{-1} up to 200°C and a second gradient of 10°C min^{-1} up to 290°C. The final temperature was held for three minutes. The transfer line temperature to the MSD was 280°C, and the ionization energy (EI) was set at 70 eV with a full scan range of 50– 300 m/z. The compounds were identified by comparing their mass spectra to the NIST 98 library using NIST mass spectral search software v2.0.

Quantitative analysis by GC-FID was performed using the same chromatographic parameters described above with the same type of column. The detector (FID) temperature was set at 280°C.

Study design

This was an open label, multicentric, single arm, observational, post-marketing surveillance study in a real-world setup.

Study duration and study centers

This study was conducted between the 1st of August 2019 and the 20th of December 2019 in discrete Indian centers.

Inclusion criteria

This study included both male and female subjects aged ≥18 years who were suffering from chronic low back pain varying in intensity.

Exclusion criteria

Subjects were excluded if they: 1) were suffering from unbearable acute pain; 2) were taking analgesic co-medication viz. antidepressants, hypnotics, muscle relaxants, anti-epileptics or corticosteroids; 3) had taken any long acting analgesics three weeks prior to enrolment; 4) had taken any short-acting analgesic viz. NSAIDs, peripheral analgesics, opioids, anaesthetics, or any other topical medication 24 hours prior to enrolment; 5) had any kidney or liver disorders; 6) had a history of epidural intervention exposure; 7) needed any other additional medication mentioned in the protocol; 8) had any hypersensitivity to the study drug; 9) were pregnant or lactating women; 10) were male and female subjects ≤ 18 years.

Methodology

Patients who attended the outpatient department of study centers and met the inclusion/exclusion criteria were considered to be eligible for the study. Demographic profile, medical assessments and evaluation parameters were recorded in a predesigned case record form (CRF) that was maintained for each subject. Eligible subjects were instructed by a medical practitioner to ingest MyrliMax® capsules as *per* the protocol. They were informed to take one capsule twice a day orally for 20 days and visit the study centre on days 0, 7, 14, and 20 in order to assess efficacy and tolerability parameters as *per* protocol. Efficacy evaluation was done by primary evaluation parameter, including measure of change in pain intensity assessed by VAS (numeric scale) on Day 0, Day 7, Day 14 and Day 20. The secondary parameter for efficacy assessment was the satisfactory score and requirement of rescue medicine. Safety and tolerability assessments were conducted by spontaneous reporting of directly observed adverse events after first dose until end treatment visit.

All subjects were advised to use NSAIDs/analgesics as a rescue medicine if required and they were asked to inform the study centre during their visit.

Statistical analysis

Data were expressed as mean±SD for pain scores as well as therapy satisfaction scores. Statistical analysis was performed using GraphPad Prism software version 8 (Graph Pad software, USA). The data of pain intensity in all subjects and subgroups were analysed using one-way ANOVA, followed by post-hoc analysis using Tukey's multiple comparison test. A p-value <0.05 was considered statistically significant. ❑

OUTCOMES

Study material analytical results

The bioactive components present in MyrliMax® capsules include curzerene, furanoeudesma-1,3-diene and lindestrene. These bioactive components are responsible for the analgesic action of the formulation. The identification and quantification as well as standardization of the bioactive furanodienes present in MyrliMax® capsules were performed using gas chromatography coupled to mass spectrometry (GC-MS) and gas chromatography coupled to a flame ionization detector (GC-FID), respectively, as *per* the procedure mentioned in the material and method section. These analytical results (Figure 1) have revealed that the total percentage of identified furanodienes was approximately 60% of the total volatile fraction, whereas the total furanodienes content was 40. 89 gm *per* kg. These results are complying with the specification of active components given by the Biosfered S.r.l. (Turin, Italy).

Clinical efficacy

A total of 204 patients (117 women and 87 men) aged between 21 and 85 (female subjects: 21-85 years; male subjects: 22-81 years), with a mean age of 49.69±13.73 years (female subjects: 50.59 ±13.13 years; male subjects: 48.51±14.49 years) were included in the study as *per* the inclusion and exclusion criteria. Table 1 lists the centers participating to the study and the number of enrolled female and male volunteers, and dropouts. Subjects' pain intensity was evaluated using VAS pain score 0-10. Subgroup analysis was conducted based on gender as well as severity score at the time of inclusion (*i.e.*, severe pain with a VAS score 7-10; moderate pain with a VAS score 4-6; and mild pain with a VAS score 1-3). Table 2 summarizes the pain score subdivision according to pain severity.

The results of our multicenter pilot study are represented in Figure 2, where data are depicted by considering both total sample data and subgroup data based on gender and pain severity. In

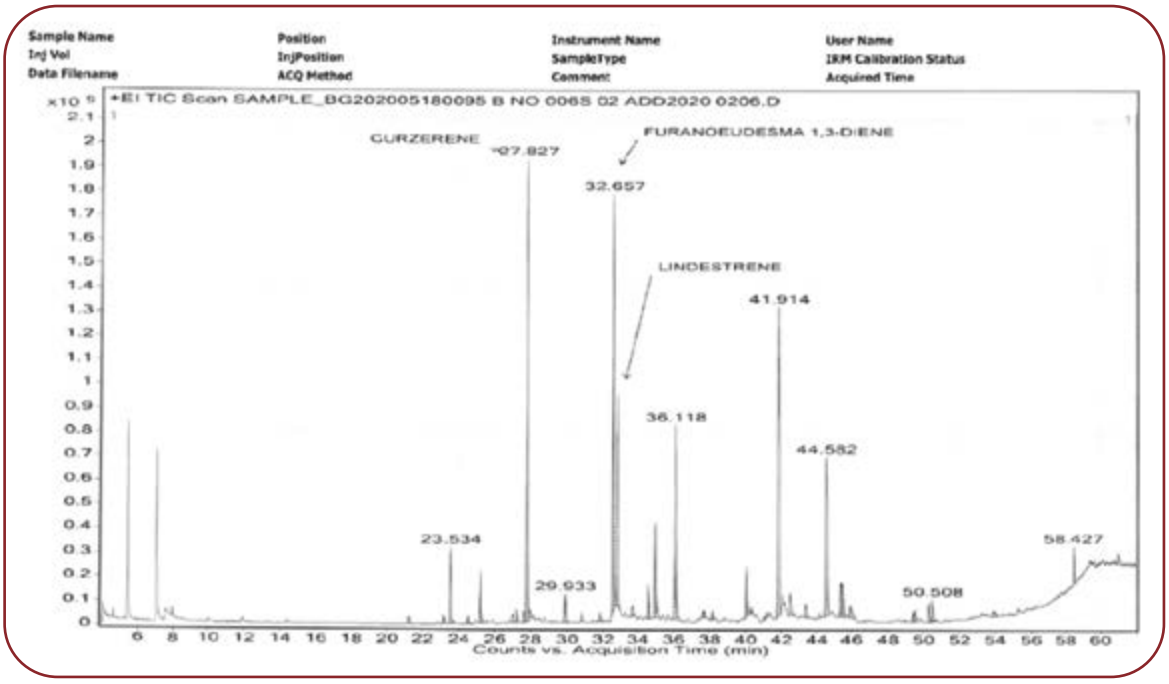

FIGURE 1. Analytical results confirming the presence of bioactive components in MyrliMax® capsules

TABLE 1. Centers involved in the pilot study and number of volunteers and dropouts *per* center

Name of center	No. of enrolled volunteers	Gender	Dropouts
Adarsh Nursing Home, Mumbai	9	9F; 0M	0
APJ multi-speciality Hospital, Walajabad.	10	5F; 5M	0
Bhargav Orthopedic Center & Banashankari Orthopedic Speciality Service, Bengaluru	9	3F; 6M	0
Diwakar Ortho & General Hospital, Jaipur	10	7F; 3M	0
Dr Jain's Clinic, Delhi	10	4F; 6M	0
Jayam Hospital, Madurai	10	3F; 7M	0
Lifespan Bone & Joint Clinic, Chennai	10	7F; 3M	0
Newlife Clinic, New Delhi	10	7F; 3M	1F; 1M
NSCB Medical College, Jabalpur	10	8F; 2M	1F; 1M
Nuha Hospital, Guntur	9	7F; 2M	0
Paravatibai Chavan Charitable trust, Mumbai.	14	14F; 0M	0
Primus Hospital, Bengaluru	10	4F; 6M	1F
Pusp Clinic, Indore	10	4F; 6M	2F
Radhika Clinic, Bengaluru	10	2F; 8M	0
Rajput Fracture, Joint & Trauma Clinic, Gwalior.	10	5F; 5M	0
Raksha Hospital, Madurai	10	2F; 8M	0
Sancheti Instiitute for Orthopaedic & Rehabilitation, Pune	10	3F; 7M	0
Sanjeevan Hospital, New Delhi	10	8F; 2M	0
Shri Kanaka Maha Laxmi Nursing Home, Vizag	10	6F; 4M	0
Suchak Hospital, Malad, Mumbai	13	9F; 4M	0
Total	204	117F; 87M	7

F=females; M=males

Pain scale	Score	Female subjects	Male subjects	Total
Mild	1 to 3	9	7	16
Moderate	4 to 6	41	33	74
Severe	7 to 10	67	47	114
Total		117	87	204

TABLE 2. Population pain score subdivision

particular, there was a significant ($p < 0.01$) decrease in pain score values for the entire population (N=204), with a progressive reduction in pain when MyrliMax® was administered. The general data for "male" and "female" subgroups showed the same decreasing trend in pain score, with no significant differences between male and female populations. With regard to pain severity, all subjects experienced a reduction in pain; thus, at the end of the administration period (day 20) there was a 73% reduction in the subgroup with initial "severe" pain, a 69% reduction in the subgroup with initial "moderate" pain, and a 90% reduction in the subgroup with initial "mild" pain. When considered separately, female subjects with initial "severe", "moderate" and "mild" score showed pain reduction by 71%, 67% and 89%, respectively, whereas male subjects with initial "severe", "moderate" and "mild" score showed pain reduction by 75%, 72% and 90%, respectively. Overall, both general and subgroup data showed similar trends in pain reduction.

We then assessed the level of therapy satisfaction in both enrolled subjects and curing physicians by setting a scale on which 0 meant lack of satisfaction, 1=poor satisfaction, 2=satisfaction and 3=high satisfaction. Figure 3 shows the result of this investigation, with a total value of almost 2.5 for the enrolled subjects and no significant differences ($p > 0.10$) in the responses of male and female subjects. Interestingly, the same value was recorded for physicians, with no statistical differences ($p > 0.3$) between physicians and subject responses.

Additionally, we evaluated each subject's opinion on MyrliMax® with respect to product ef-

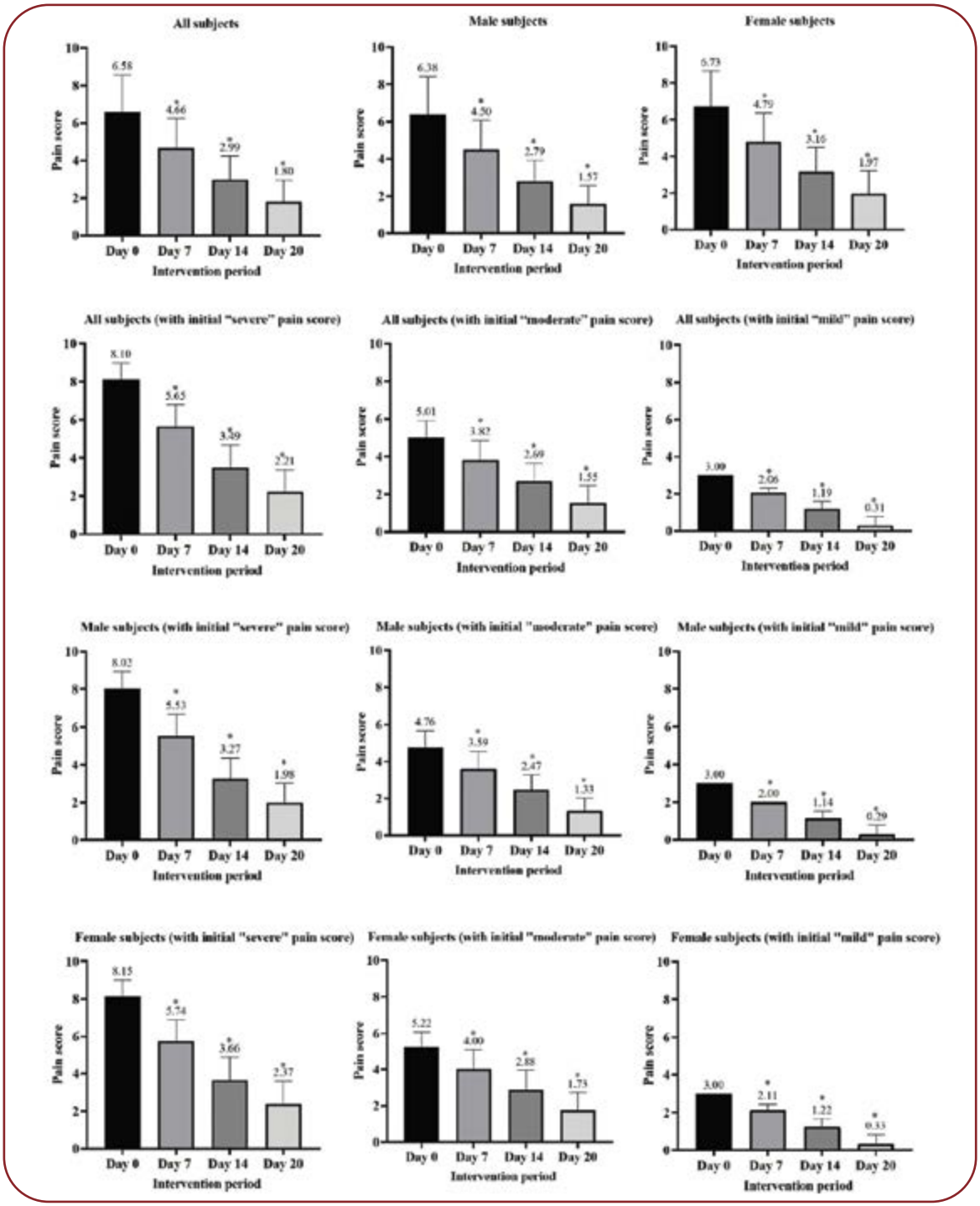

FIGURE 2. VAS pain scores (mean±SD) for female, male and female + male subjects during the 20 days of MyrliMax® administration; *significant ($p < 0.01$) differences with respect to day 0

ficacy. The results of this investigation are shown in Figure 4, where 55% of the total population showed a high satisfaction, followed by a 38% of subjects who declared satisfaction for the product meaning 93% of total population showed satisfaction or higher satisfaction with MyrliMax® therapy. A minority of the general population (5%) was poorly satisfied, whereas only one subject was not satisfied. The separation of population data based on gender showed a higher satisfaction for males (62%) when compared to females (49%); the latter also showed a lower percentage of subjects

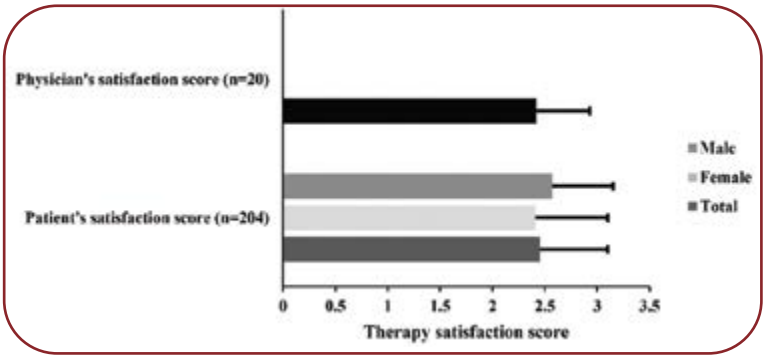

FIGURE 3. Therapy satisfaction scores (mean±SD) of MyrliMax® capsule administration in subjects and physicians expressed as 0=not at all satisfied; 1=poorly satisfied; 2=satisfied; 3=highly satisfied. Metric bars represent standard deviation (SD).

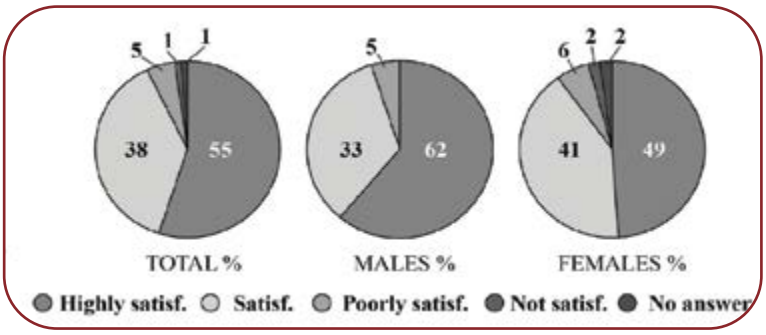

FIGURE 4. Subjects' opinion – total and gender-based satisfaction of MyrliMax® capsule efficacy expressed as percentage values

declaring a poor satisfaction and no satisfaction (six and two subjects, respectively).

Finally, the average number of rescue medicine units consumed *per* subject during particular periods of study (first week, second week and third week) were also evaluated. The findings were summarized in Table 3, where subjects required rescue medicine support during the first week of therapy, and this requirement gradually reduced during the following weeks. Male subjects needed less rescue medicines during second week compared to female subjects. This observation is in line with the general assumption about sensitivity of women towards pain. Results also highlight a potential requirement for rescue medicines during early 2-4 days while on MyrliMax® capsule therapy. Reduction in rescue medicine requirement during weeks 2 and 3 of MyrliMax® capsule therapy may point to a reduced need or dependency on synthetic pharmaceutical dosages. In most cases, the rescue medicines included Paracetamol, NSAIDs (Ibuprofen/Diclofenac/Aceclofenac) or Tramadol.

TABLE 3. Average number of rescue medicine units consumed *per* subject during the study

Study period	All subjects	Female subjects	Male subjects
First week	5.9	5.73	6.14
Second week	2.12	2.99	0.98
Third week	0.52	0.56	0.48

Tolerability

There were no reports of significant serious adverse events due to study treatment, which indicated that the treatment with MyrliMax® was well-tolerated by participants. Few mild side effects were observed in eight patients, including mild nausea (n=4), vomiting (n=2), and loose motion (n=1). Also, one patient showed symptoms of vertigo. However, these side effects occurred during the early course of therapy in most cases, and none of the observed side effects disrupted treatment. Seven dropouts occurred during the study, which were not corelated to treatment induced side effects or tolerability issues. ❑

DISCUSSION

Evidence on efficacy of *C. myrrha* (Myrrha, Syn. *C. molmol*) gum resin extract in treatment of discrete pain types have been scrutinized in several clinical studies. *C. myrrha* contains a bioactive component, furanodienes, which shows analgesic and anti-inflammatory actions. The furanodienes component (curzerene and furanoeudesma-1, 3-diene) of *C. myrrha* was reported to exert an analgesic activity by interacting with opioid receptor, which was confirmed by reversal of this action by naloxone (13). Myrrh had been also reported to have a potential role on inflammatory targets such as COX, NO formation, ROS, TNF-α, PGE-2, NF-κB, MAPK, and it was showed to have an anti-inflammatory action (15). A prospective open label study for prophylaxis of migraine reported the effectiveness of *C. myrrha* treatment because of its analgesic and anti-inflammatory activities (16). A long-term pilot study with a duration of six months was conducted in patients suffering from migraine without aura or tension type headache. In this study, patients received a nutraceutical-based combination containing MyrLiq®, a highly standardized gum resin extract of *C. myrrha*, which was found to lead to an improvement in pain and a significant reduction in the levels of several cytokines

(IL-6, IL-8 and TNF-α). This study also reported the safety of *C. myrrha* extract for a longer period of time (17). Nutraceutical supplement containing *C. myrrha* was reported to improve various types of tendinopathies when administered along with extracorporeal shock wave therapy (ESWT). The results of this study showed the effectiveness of supplement containing myrrh in faster pain relief, which was evaluated by VAS score. Also, no side effects were observed with the administration of nutraceutical supplement (18). A pilot study on the analgesic effects of highly standardized gum resin extract of *C. myrrha* with a high furanodienes content reported pain alleviation at 400 mg and 200 mg in various etiologies of pain. In this study, a dose of 400 mg *per* day was effective in all kinds of pain, whereas 200 mg *per* day alleviated only low back pain in male subjects and fever dependent pain in all patient, showing its significant analgesic properties (14). Also, *C. myrrha* extract showed efficacy in reducing the number of days with headache, average pain intensity and analgesic consumption when combined with *Ginkgo biloba*, CoQ10 and riboflavin in women suffering from menstrual migraine (19). In women suffering from endometriosis, *C. myrrha* extract in combination with alpha-lipoic acid and palmitoilethanolamide led to a significant reduction in pain symptoms including dyspareunia, dysmenorrhoea and chronic pelvic pain (20). In patients suffering from chronic pain affecting muscles, joints or the back due to sports trauma or advanced age, *C. myrrha* extract was found to determine a significant reduction in pain perception (just within three days) as well as loss of functions, with good tolerability profile (21). In patients with mild osteoarthritis, *C. myrrha* extract in combination with chondroprotective agents such as glucosamine, chondroitin, curcuma and bromelain led to a significant reduction in joint pain and stiffness. In this study, the intervention period of six months indicates the safety of oral *C. myrrha* gum resin extract for long-term use (22). In patients with recurrent uncomplicated urinary tract infections, *C. myrrha* extract is useful in preventing symptomatic urinary tract infection episodes and improves quality of life (23). In patients with symptoms of acute diarrhoea, *C. myrrha* extract in combination with coffee charcoal and chamomile flower extract showed its efficacy and safety (24). *C. myrrha* extract was found to be effective in reducing mild to moderate chronic pain in elderly population when combined with *Piper nigrum* and *Rosmarinus officinalis* (25). The fact that *C. myrrha* extract did not cause any significant side effects even at a higher dose of 11.5 mg/kg body weight *per* day on liver and kidney function test indicates its safety even at a higher dose (26).

Although many trials confirmed the efficacy of *C. myrrha* extract, there were no clinical studies in Indian population. Our study was an open label pilot study that demonstrated the efficacy of MyrliMax® capsules containing a highly standardized extract of *C. myrrha* in gastro protectant delayed release capsule in Indian patients suffering from chronic low back pain. In this study, quantitative and qualitative standardization of the extract for bioactive furanodienes was done using GC-MS and GC-FID. Our findings were consistent with those provided by previous studies and confirmed the effectiveness of *C. myrrha* extract as an analgesic agent. The results of the present study reported a significant reduction in pain scores at every treatment interval in both overall population and subgroups (based on "severity" and "gender"). Therapy satisfaction was assessed for both patients and physicians and showed a high level of satisfaction, with no significant differences between patient and physician scores, as highlighted in Figure 2. This study also showed that the administration of MyrliMax® capsule could reduce concomitant use and need of other rescue medication required for pain. Safety assessment showed the better tolerability of the MyrliMax® capsule. Collectively, the results of present study highlight the effectiveness and safety of MyrliMax® capsule in alleviating LBP of different intensity. We believe that the significant efficacy of MyrliMax® capsules observed in this study at lower dose is due to the usage of gastro-protectant delayed release capsule dosage form that prevents gastric interaction of bioactive furanodienes and allows its release in intestinal fluid for further absorption and biological actions. ❑

CONCLUSION

MyrliMax® capsule is a potentially effective and safe therapy for pain reduction in patients suffering from chronic low back pain. Since an open label, non-randomized, non-controlled design may be a major limitation of this trial, ran-

domised trials with controlled designs are needed to further explore the wider role of *C. myrrha* extract based formulations in the management of chronic painful inflammatory conditions. ❑

Conflicts of interest: Varun SUREJA, Dharmeshkumar KHENI, Mayank RAJAWAT and Ajit MAGAR are employees of Sundyota Numandis Group of Companies. Divyanshu PRAJAPATI and Asha KRISHNARAJ were employees of Sundyota Numandis Group of Companies during the course of this study.

Financial support: none declared.

Acknowledgements: We acknowledge the support of Professor Massimo Maffei, University of Turin, Italy, for his advice in preparing the manuscript. We are grateful to late Dr. Virat Chavan-Parvatibai Chavan Charitable Trust, Mumbai, for his contribution to conducting this study.

References

1. **Houze B, El-Khatib H, Arbour C.** Efficacy, tolerability, and safety of non-pharmacological therapies for chronic pain: An umbrella review on various CAM approaches. *Progr Neuropsychopharmacol Biol Psychiatry* 2017;79(Pt B):192-205.
2. **Hartvigsen J, Hancock MJ, Kongsted A, et al.** What low back pain is and why we need to pay attention. *Lancet* 2018;10137:2356-2367.
3. **Petzke F, Klose P, Welsch P, et al.** Opioids for chronic low back pain: An updated systematic review and meta-analysis of efficacy, tolerability and safety in randomized placebo-controlled studies of at least 4 weeks of double-blind duration. *Eur J Pain* 2020;3:497-517.
4. **Meier ML, Vrana A, Schweinhardt P.** Low Back Pain: The Potential Contribution of Supraspinal Motor Control and Proprioception. *Neuroscientist* 2019;6:583-596.
5. **Smith E, Hoy DG, Cross M, Vos T, et al.** The global burden of other musculoskeletal disorders: estimates from the Global Burden of Disease 2010 study. *Ann Rheum Dis* 2014;8:1462-1469.
6. **Andersson GBJ.** Epidemiology of low back pain. *Acta Orthopaedica Scandinavica* 1998;69:28-31.
7. **Stafford MA, Peng P, Hill DA.** Sciatica: a review of history, epidemiology, pathogenesis, and the role of epidural steroid injection in management. *British Journal of Anaesthesia* 2007;4:461-473.
8. **Rekatsina M, Paladini A, Piroli A, et al.** Pathophysiologic Approach to Pain Therapy for Complex Pain Entities: A Narrative Review. *Pain* Ther 2020;1:7-21.
9. **Mathieson S, Kasch R, Maher CG, et al.** Combination Drug Therapy for the Management of Low Back Pain and Sciatica: Systematic Review and Meta-Analysis. *Journal of Pain* 2019;1:1-15.
10. **Moore RA, McQuay HJ.** Prevalence of opioid adverse events in chronic non-malignant pain: systematic review of randomised trials of oral opioids. *Arthritis Research & Therapy* 2005;5:R1046-R51.
11. **Ong CK, Lirk P, Tan CH, Seymour RA.** An evidence-based update on nonsteroidal anti-inflammatory drugs. *Clin Med Res* 2007;1:19-34.
12. **Su SL, Wang TJ, Duan JA, et al.** Anti-inflammatory and analgesic activity of different extracts of Commiphora myrrha. *J Ethnopharmacol* 2011;2:251-258.
13. **Dolara P, Luceri C, Ghelardini C, et al.** Analgesic effects of myrrh. *Nature* 1996;6560:29.
14. **Germano A, Occhipinti A, Barbero F, Maffei ME.** A Pilot Study on Bioactive Constituents and Analgesic Effects of MyrLiq (R), a Commiphora myrrha Extract with a High Furanodiene Content. *Biomed Res Int* 2017;2017:3804356.
15. **Shen T, Li G-H, Wang X-N, Lou H-X.** The genus Commiphora: a review of its traditional uses, phytochemistry and pharmacology. *J Ethnopharmacol* 2012;2:319-330.
16. **Tonini MC, Giordano L.** Commiphora myrra, alternative treatment in migraine prophylaxis: open label prospective pilot study. *Neurol Sci* 2018;39(Suppl 1):165-166.
17. **Scarzella L.** Effects of a novel MYRLIQ®, Ginkgo Biloba, Q10 and vitamin B2 (riboflavin) based nutra-ceutical in patients suffering from migraine headache without aura or sporadic episodes of tension-type headache. A six-month pilot study. *Gazzetta Medica Italiana, Archivio per le Scienze Mediche* 2017;4:149-153.
18. **Vitali M, Naim Rodriguez N, Pironti P, et al.** ESWT and nutraceutical supplementation (Tendisulfur Forte) vs ESWT-only in the treatment of lateral epicondylitis, Achilles tendinopathy, and rotator cuff tendinopathy: a comparative study. *J Drug Assess* 2019;1:77-86.
19. **Mostardini C.** Use of nutraceutical Clevia, in Pure Menstrual Migraine. *J Headache Pain* 2017;18(Suppl 1):P45.
20. **Leo VD, Cagnacci A, Cappelli V, et al.** Role of a natural integrator based on lipoic acid, palmitoiletanolamide and myrrh in the treatment of chronic pelvic pain and endometriosis. *Minerava Ginecol* 2019;3:191-195.
21. **Pierro FD, Bertuccioli A, Giuberti R.** Analgesic effects of RodeMyr®, a Commiphora molmol extract with a highly standardized furanodiene content. *Nutrafoods* 2019;2:95-99.
22. **Vianello R.** Efficacy and safety of DIAGO® Artiplus a chondroprotective agent in patients with joint pain and stiffness: a 6 months prospective study. *Int J Exp Clin Res* 2016;5:5-8.
23. **Cai T, Tiscione D, Cocci A, et al.** Hibiscus extract, vegetable proteases and Commiphora myrrha are useful to prevent symptomatic UTI episodes in patients affected by recurrent uncomplicated urinary tract infections. *Archivio Italiano di Urologia e Adnrologia* 2018;3:203-307.
24. **Albrecht U, Muller V, Schneider B, Stange R.** Efficacy and safety of a herbal medicinal product containing myrrh, chamomile and coffee charcoal for the treatment of gastrointestinal disorders: a non-interventional study. *BMJ Open Gastro* 2014;1:e000015.
25. **Gianni W, Carlo MD, Colangelo L, et al.** Short-term efficacy of a fixed association of Palmitoylethanolamide and other phytochemical as add-on therapy in the management of chronic pain in elderly patients;a real-world retrospective study. *Geriatric Care* 2018;4:7177.
26. **Abdul-Ghani RA, Loutfy N, Hassan A.** Myrrh and trematodoses in Egypt: an overview of safety, efficacy and effectiveness profiles. *Parasitol Int* 2009;3:210-214.