Section A-Research paper
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The Effectiveness of XtraBos™ in Osteoarthritis and its Comorbidities in an In-Home User Trial (iHUT)

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Abstract:

Introduction: Osteoarthritis (OA) is a prevalent musculoskeletal condition associated with significant pain, functional limitations, and reduced quality of life. Comorbidities like hypertension (HT), neuropathic pain (NP) and insomnia frequently coexist with OA. Addressing these conditions alongside OA treatment can improve pain management and enhance overall well-being. By targeting NP and sleep disorders, healthcare professionals can enhance treatment outcomes and patient compliance in OA management. Boswellia serrata extracts, including 3-O-acetyl-11-keto-beta-boswellic acid (AKBA), have been found to be beneficial in OA recently. AKBA has also been found beneficial in many comorbidities of OA, especially HT. Boswellia serrata is known for its potent anti-inflammatory properties. The resin extracted from this plant contains bioactive compounds, such as 3-O-acetyl-11-keto-β-boswellic acid (AKBA), which have been extensively studied for their ability to combat inflammation. This study aims to investigate the efficacy and safety of XtraBos™, a herbal nutraceutical product, which is a standardised Boswellia serrata extract, in the management of OA and its comorbidities. It assessed the changes in the symptoms of OA, neuropathic pain & insomnia.

Materials and Methods: An iHUT study was conducted to investigate the efficacy of XtraBos™ (standardised to contain 30% AKBA & 85% Boswellic acids), in individuals with OA and comorbidities such as hypertension, insomnia and neuropathic pain . The trial lasted for 13 weeks, with individuals receiving an oral administration of XtraBos™ capsules twice daily at a dosage of 125 mg. Outcome assessments were conducted to evaluate the impact of XtraBos™ on OA symptoms and the respective comorbidities. Data collection was performed through questionnaire administered at specific intervals, allowing for the comprehensive evaluation of the treatment's effectiveness on the complaints and comorbidities. The iHUT

setting of the trial, provided a real-life context for assessing the product's efficacy and user experience.

Results: A diverse population of 151 individuals aged 18 to 65 volunteered for the study out of which 112 respondents completed the study. 39 respondents were excluded due to non-compliance. Treatment with XtraBos™, which is capsule containing extract obtained from Boswellia serrata standardised to 30% AKBA and 85% Boswellic acids, demonstrated an overall gradual decrease in the symptoms. After 13 weeks, it was observed in the total population that 84 patients (75%) showed reduction in their joint pains, 75 patients (66.9%) showed improvement in their sleep quality and 79 patients (70%) showed reduction in NP. Due to practical reasons variations in blood pressure was not monitored. It was observed that OA patients with HT (group 1) showed reduction in joints and sleep complaints. Similarly, OA patients with NP (group 3) showed improvements in joint and NP symptoms. However, in the case of OA patients with insomnia (group 2) showed no significant reduction in their sleep complaints though the joint pain was improved. Amongst all, 6 individuals documented minor reactions, with ambiguity regarding their correlation with the treatment product. These findings highlight the potential efficacy of XtraBos™ in improving joint symptoms, managing insomnia, and alleviating neuropathic pain in individuals with OA.

Conclusion: This iHUT highlights the potential efficacy of XtraBos™, in improving symptoms and quality of life for individuals with OA and associated conditions. Although it improves OA symptoms in insomnia subjects, it does not mend their sleep quality as such. Further analysis including in-vitro studies and randomised controlled trials will provide a comprehensive assessment, potentially informing personalized treatment approaches and enhancing OA management strategies.

Keywords: Osteoarthritis, Boswellia serrata, AKBA, XtraBos™, Osteoarthritis with hypertension, Osteoarthritis with neuropathic pain, Osteoarthritis with insomnia.

1. Introduction

For thousands of years, the plant extract known as Boswellia serrata, frequently referred to as Indian frankincense, has been a crucial part of Ayurvedic treatment. Various systemic and local inflammatory illnesses have been treated with it historically in folk medicine. Recent experimental evidence from both human and animal research suggests that Boswellia serrata has the potential to cure a number of inflammatory diseases, including inflammatory bowel disease (IBD), rheumatoid arthritis (RA), osteoarthritis (OA), and asthma.[1] OA is a

degenerative joint disease that affects millions of people worldwide, leading to chronic pain and functional limitations. XtraBos™, an extract obtained from Boswellia serrata standardized to 30% AKBA (3-O-acetyl-11-keto-β-boswellic acid) and 85% Boswellic acids, has shown promising results in the management of osteoarthritis (OA).[2] It is characterized by the breakdown of articular cartilage, subchondral bone changes, and joint inflammation.[3] The disease primarily affects weight-bearing joints such as the knees, hips, and spine, but can also involve other joints like the hands and feet.[4] Age, obesity, joint injury, and repetitive mechanical stress are known risk factors for OA.[5] While OA is traditionally considered a cartilage disease, recent research has highlighted the involvement of other joint tissues, such as the synovium, subchondral bone, and ligaments, in its pathophysiology.[6]

The classic symptoms of OA often co-exist with some other underlying diseases. These frequently occurring comorbidities in individuals with OA can be both musculoskeletal and systemic in nature.[7] Musculoskeletal comorbidities include conditions such as osteoporosis, gout, and rheumatoid arthritis, which can influence the progression and management of OA.[8] Systemic conditions commonly associated with OA include obesity, metabolic syndrome, and cardiovascular diseases including hypertension (HT). Bidirectional relationships have been observed between these conditions and OA, with obesity playing a significant role in the development and progression of OA due to increased stress on weight-bearing joints.[9]

In addition to the typical symptoms of joint pain, stiffness, and reduced range of motion, some individuals with OA also experience neuropathic pain (NP). NP in OA arises from nerve sensitization and altered pain processing mechanisms, resulting in heightened pain sensations, increased sensitivity, and abnormal sensations like tingling or burning.[10] The exact mechanisms underlying NP in OA are not fully understood, but structural changes within the joint and peripheral and central sensitization processes are thought to play a role.[11] Sleep disturbances frequently coexist with chronic pain conditions, including OA.[12] The relationship between OA and sleep disturbances is bidirectional and complex. Moreover, the pain and physical discomfort associated with OA can directly interfere with sleep, making it difficult to find a comfortable position and maintain restful sleep.[13] On the other hand, sleep disturbances themselves can worsen pain perception in individuals with OA. Sleep deprivation and poor sleep quality can contribute to central sensitization, amplifying pain perception and lowering pain thresholds.[14] Disrupted sleep can also lead to fatigue, impaired mood, and reduced pain coping mechanisms, further contributing to a cycle of pain and sleep disturbances.[15] Hypertension, or high blood pressure, can contribute to this reduced blood

flow by causing damage to the blood vessels and narrowing their diameter. This reduced blood flow can have negative effects on joints affected by OA.[16] Comorbidities in individuals with OA necessitate a comprehensive and multidisciplinary approach to management, addressing modifiable risk factors and considering the potential impacts on overall health and well-being.[20]

Multiple recent findings, have established that Boswellia serrata extracts, specifically 3-O-acetyl-11-keto-beta-boswellic acid (AKBA), confer benefits in the context of osteoarthritis (OA). AKBA, the bioactive compound found in Boswellia serrata, has been extensively studied for its potential role in the management of OA.[21] It exhibits anti-inflammatory properties by inhibiting the production of pro-inflammatory enzymes and reducing the synthesis of inflammatory mediators.[22] AKBA also possesses analgesic properties, modulating pain pathways and providing pain relief in individuals with OA.[23] Additionally, it can protect and preserve joint cartilage by inhibiting enzymes that contribute to cartilage breakdown and by exerting antioxidant effects to reduce oxidative damage in the joints.[24] Studies have demonstrated the efficacy of AKBA in improving OA symptoms and functional outcomes, comparable to non-steroidal anti-inflammatory drugs but with fewer side effects.[25] However, more research is needed to establish long-term safety, and potential synergistic effects with other treatments.[26] The investigation of Boswellia serrata, in individuals with OA and comorbidities such as neuropathic pain and sleep disorders holds significance in understanding its effectiveness and potential benefits. Hence, an in-home user trial was planned to evaluate its efficacy and safety in OA and also in its co-morbidities HT, NP & insomnia. The findings from this research can contribute to the development of evidence-based treatment strategies and assist healthcare professionals and patients in making informed decisions regarding its use as a potential therapeutic option.[27] However, OA is a complex and challenging disease that affects a substantial portion of the population. The Boswellia serrata extract, XtraBos™ (standardised to contain 30% AKBA & 85% Boswellic acids), offers a potential alternative or adjunct therapy for individuals seeking a natural approach to managing OA symptoms. It has shown anti-inflammatory, analgesic, and cartilage-protective properties. Comorbidities commonly observed in individuals with OA further highlight the need for a comprehensive management approach. This study aims to investigate the efficacy and safety of XtraBos™, in individuals with OA and comorbidities, and assess the changes in the symptoms of OA, NP & insomnia, providing valuable insights for improved symptom control and enhanced quality of life.[28]

2. Materials and Methods

2.1 Study Design

The study was conducted between January 2023 – April 2023, for 91 days as an experimental In-Home Use Trial ("iHUT") of Boswellia serrata extract XtraBos™, in 151 volunteers with specified selection criteria. By utilizing the iHUT setting in the trial, the opportunity to evaluate the product's efficacy and user experience within a real-life context was offered. Volunteers between the ages of 18 and 65 who do not suffer from allergies on the body or face and do not have any specified skin conditions are eligible for this study. Additionally, both male and female volunteers pre-diagnosed with osteoarthritis were included in the study. By selecting patients who meet these criteria, the study aimed to gather data from individuals who represented the target population and could provide valuable insights into the efficacy and safety of XtraBos™ in managing osteoarthritis and its associated comorbidities.

2.3 Data Collection

The study involved the recruitment and selection of volunteers from a panel of profiled Clicks Research users. The online methodology was employed throughout the process, including the recruitment, execution, and collection of raw data. Volunteers were primarily recruited through Search Engine Optimization (SEO) techniques and referrals from other volunteers. The selection of volunteers was based on positive data matching against predefined profile criteria. Once identified as eligible, volunteers were invited to participate in the study via email and had the choice to voluntarily accept or decline the invitation. All the volunteers who agreed to participate in the study were included in the data collection process. Their inclusion was contingent upon submitting a questionnaire after following the study directions. Each volunteer provided their responses online, answering questions related to OA and the comorbidities in relation to the product being investigated. This approach ensured a systematic and standardized collection of data from the recruited volunteers.

2.4 Breakdown of Respondents

Out of 151 volunteers, 130 responses were received at the beginning of the study. Actions taken with non-respondents were documented during the data collection process. Finally, 112 responded to the questionnaire and completed the 13 week study, resulting in a response rate of approximately 74%. The remaining 39 respondents were excluded from the study due to their failure to fulfill one or more of their contractual obligations. These actions were taken to ensure the integrity and reliability of the study results. In addition, it was noted that six out of the 151 respondents reported adverse reactions. The adverse reactions were carefully

documented and analyzed as part of the study's assessment of safety and potential side effects.

2.5 Study Process

2.5.1 Enrollment

The enrollment process in our research study played a crucial role in recruiting and selecting patients. For patients selection, we employed eligibility criteria based on specific demographics and medical factors, using positive data matching to identify eligible volunteers. Once identified, eligible patients received detailed email invitations explaining the research objectives, procedures, potential risks and benefits, and the voluntary nature of participation. Informed consent was obtained from all patients prior to their inclusion in the study.

Table 1: Questionnaire used for the patients

Questionnaire
Question 1: My joint pain feels reduced
Question 2: My joint stiffness feels reduced
Question 3: My morning joint stiffness feels reduced
Question 4: My joint swelling appears reduced
Question 5: My mobility feels improved
Question 6: My joint pain while sitting feels improved
Question 7: My joint pain whilst lying down feels improved
Question 8: I find it easier to fall asleep
Question 9: I find it easier to stay asleep
Question 10: I no longer wake up too early
Question 11: My sleep quality feels improved
Question 12: I find it easier to function during day-to-day tasks
Question 13: My neuropathic pain feels reduced
Question 14: If you were to write a review of this product, what would you say?

(Subjective)

Data collection was conducted through online questionnaires, where patients were instructed to provide responses for each product or item being investigated. The questionnaire was designed to align with the research objectives, ensuring relevant data collection. It contained 7 questions about OA, 5 about sleep disorders and 1 for NP. The questionnaire was regularly employed to evaluate the impact of XtraBos™ on symptoms and comorbidities associated with OA, with the exception of HT, due to practical considerations. Clear and comprehensive instructions were provided to patients to facilitate accurate and consistent data submission. The scaling, ranging from 1 to 9, presents a comprehensive spectrum of responses, progressing from "Strongly Disagree" (1) to "Strongly Agree" (9). This extended scale allows patients to express varying degrees of agreement or disagreement, enabling a nuanced and accurate representation of their opinions and perceptions. By implementing this enrollment process, we were able to establish a diverse patients pool, enabling us to gather valuable data for analysis and evaluation.

2.5.2 Safety Assessment

A comprehensive safety assessment was conducted throughout the study to monitor and evaluate the well-being of patients. This assessment included measures such as adverse event reporting, regular health monitoring, compliance monitoring, and adherence to ethical considerations. Patients were instructed to report any adverse events, and their health status was closely monitored during the 13-week treatment period. For a comprehensive analysis, patients were requested to provide thorough details concerning any adverse events encountered. Compliance with the dosage regimen was assessed, and ethical guidelines were followed to protect patients rights. The safety assessment provided valuable insights into potential risks and benefits, ensuring patients safety and well-being throughout the study.

2.6 Data Analysis

The data analysis process involved the utilization of online methods, including Search Engine Optimization and referrals, to successfully target and engage potential patients from a diverse pool of profiled Clicks Research users. The collected dataset encompassed responses from a total of 151 individuals for about 13 weeks. This approach ensured the inclusivity and representativeness of our sample, contributing to the relevance of the data for analysis.

2.6.1 Groups/Population

The recruitment process targeted specific groups of volunteers for the study:

Group 1: Volunteers with osteoarthritis and hypertension (HT).

Group 2: Volunteers with osteoarthritis and insomnia or other sleep disorders.

Group 3: Volunteers with osteoarthritis and neuropathic pain (NP).

The study enrolled 52 volunteers in Group 1, resulting in 34 responses, 50 volunteers in Group 2, resulting in 40 responses, and 49 volunteers in Group 3, resulting in 38 responses. These distinct groups enabled a comprehensive investigation into the effects of AKBA treatment on various conditions associated with osteoarthritis.

2.6.2 Statistical Analysis

The statistical analysis of the collected data involved the application of the Chi-Squared Test to assess the significance of relationships between patients' responses and the given scaling parameters. The scaling parameters included a range of options from 1 to 9, with descriptions ranging from "Not Satisfied" to "Satisfied." The Chi-Squared Test was also employed to uncover potential associations between patients' perceptions and their demographic characteristics, offering insights into the correlation between treatment outcomes and individual attributes.

3. Results

A total of 151 individuals volunteered for the study. Out of 151 volunteers, 130 responses were received at the beginning of the study. The recruitment targeted specific groups, including 52 volunteers with osteoarthritis and HT (group 1) resulting in 34 responses, 50 volunteers with osteoarthritis and insomnia and other sleep disorders resulting in 40 responses (group 2), and 49 volunteers with osteoarthritis and NP (group 3) resulting in 38 responses. The results of the XtraBos™ study demonstrated significant improvements in various aspects of OA symptoms, its comorbidities over the 13-week treatment period. The data was recorded at the intervals of 2 weeks in the order 2 weeks, 4 weeks, 8 weeks, 10 weeks, 12 weeks and the final assessment in 13 weeks. 13 questions from the questionnaire (Table 1) were analysed at the specified intervals, which reflected improvement in various segments. By the end of the 13-week treatment period, patients reported significant improvements in all measured aspects of OA symptoms and functional outcomes. Joint pain, joint stiffness, morning joint stiffness, joint swelling, mobility, joint pain while sitting, joint pain while lying down, sleep initiation, staying asleep, not waking up too early, sleep quality, the ability to function during day-to-day tasks, and neuropathic pain were all significantly improved at the end of 13 weeks compared to 2 weeks (as shown in table 2). The data was collected in 9 point scale but segregated into the categories ‘Satisfied’, ‘Neutral’ and ‘Not Satisfied’ for easy assessment. Prior to the data collection, 66% & above was assigned as the

'Pass mark' in order to substantiate the claims. Similar distribution of individual scores for group 1, group 2 and group 3 patients has been depicted in table 3, 4 and 5 respectively.

Table 2: Total population distribution of scores comparing after 2 weeks of treatment to final week (n=112). Asterisk (*) next to the 'Satisfied' % represents the % of patients that marked 'Satisfied' score >= 'Pass mark' (66%).

	After 2 weeks of treatment % (2 weeks)			**Final % (13weeks)**		
Questionnaire	**Satisfied**	**Neutral**	**Not Satisfied**	**Satisfied**	**Neutral**	**Not Satisfied**
Q 1. My joint pain feels reduced	55.38	32.31	12.31	75*	9.82	15.18
Q2. My joint stiffness feels reduced	51.54	33.08	15.38	75.89*	8.04	16.07
Q3. My morning joint stiffness feels reduced	56.38	25.38	19.23	73.21*	11.61	15.18
Q4. My joint swelling appears reduced	44.54	38.66	16.81	72.64*	12.26	15.09
Q5. My mobility feels improved	53.85	33.08	13.08	75.89*	12.5	11.61
Q6. My joint pain while sitting feels improved	54.62	32.31	13.08	75*	9.82	15.18
Q7. My joint pain while lying down feels improved	50	30	20	71.43*	14.29	14.29
Q8. I find it easier to fall asleep	53.85	28.46	17.69	67.86*	17.86	14.29
Q9. I find it easier to stay asleep	53.08	29.23	17.69	64.29	23.21	12.5
Q10. I no longer wake	40.77	37.69	21.54	63.39	18.75	17.86

up too early						
Q11. My sleep quality feels improved	52.31	26.92	20.77	66.96*	18.75	14.29
Q12. I find it easier to function during day-to day tasks	57.69	27.69	14.62	76.79*	10.71	12.5
Q13. My neuropathic pain feels reduced	45.24	39.68	15.08	74.11*	10.71	15.18

Table 3: Distribution of scores comparing after 2 weeks of treatment with final week for group 1 (n=34). Asterisk (*) next to the 'Satisfied' % represents the % of patients that marked 'Satisfied' score >= 'Pass mark' (66%).

	After 2 weeks of treatment % (2 weeks)			**Final % (13weeks)**		
Questionnaire	**Satisfied**	**Neutral**	**Not Satisfied**	**Satisfied**	**Neutral**	**Not Satisfied**
Q 1. My joint pain feels reduced	55.88	29.41	14.71	79.41*	5.88	14.71
Q2. My joint stiffness feels reduced	55.88	26.47	17.65	73.53*	11.76	14.71
Q3. My morning joint stiffness feels reduced	61.76	23.53	14.71	70.59*	14.71	14.71
Q4. My joint swelling appears reduced	55.17	37.93	6.9	71.88*	15.62	12.5
Q5. My mobility feels improved	55.88	32.35	11.76	79.41*	11.76	8.82
Q6. My joint pain while sitting feels improved	55.88	35.29	8.82	76.47*	8.82	14.71

Q7. My joint pain while lying down feels improved	44.12	41.18	14.71	73.53*	14.71	11.76
Q8. I find it easier to fall asleep	47.06	38.24	14.71	61.76	26.47	11.76
Q9. I find it easier to stay asleep	44.12	35.29	20.59	55.88	35.29	8.82
Q10. I no longer wake up too early	35.29	38.24	26.47	55.88	32.35	11.76
Q11. My sleep quality feels improved	38.24	38.24	23.53	67.65*	20.59	11.76
Q12. I find it easier to function during day-to day tasks	55.88	32.35	11.76	76.47*	14.71	8.82
Q13. My neuropathic pain feels reduced	41.94	45.16	12.9	74.19*	9.68	16.13

Table 4: Distribution of scores comparing after 2 weeks of treatment with final week for group 2 (n=40). Asterisk (*) next to the 'Satisfied' % represents the % of patients that marked 'Satisfied' score >= 'Pass mark' (66%).

	After 2 weeks of treatment % (2 weeks)			**Final % (13weeks)**		
Questionnaire	**Satisfied**	**Neutral**	**Not Satisfied**	**Satisfied**	**Neutral**	**Not Satisfied**
Q 1. My joint pain feels reduced	62.5	30	7.5	72.5*	15	12.5
Q2. My joint stiffness feels reduced	60	30	10	75*	10	15
Q3. My morning joint stiffness feels	65	22.5	12.5	72.5*	15	12.5

reduced						
Q4. My joint swelling appears reduced	48.72	38.46	12.82	76.92*	12.82	10.26
Q5. My mobility feels improved	62.5	27.5	10	72.5*	20	7.5
Q6. My joint pain while sitting feels improved	60	30	10	72.5*	17.5	10
Q7. My joint pain while lying down feels improved	62.5	20	17.5	75*	12.5	12.5
Q8. I find it easier to fall asleep	72.5*	7.5	20	75*	10	15
Q9. I find it easier to stay asleep	67.5*	15	17.5	75*	12.5	12.5
Q10. I no longer wake up too early	57.5	17.5	25	72.5*	12.5	15
Q11. My sleep quality feels improved	67.5*	10	22.5	72.5*	12.5	15
Q12. I find it easier to function during day-to day tasks	70*	17.5	12.5	75*	12.5	12.5
Q13. My neuropathic pain feels reduced	45	47.5	7.5	75.68*	18.92	5.41

Table 5: Distribution of scores comparing after 2 weeks of treatment with final week for group 3 (n=38). Asterisk (*) next to the 'Satisfied' % represents the % of patients that marked 'Satisfied' score >= 'Pass mark' (66%).

	After 2 weeks of treatment % (2 weeks)			**Final % (13weeks)**		
Questionnaire	**Satisfied**	**Neutral**	**Not Satisfied**	**Satisfied**	**Neutral**	**Not Satisfied**

Q 1. My joint pain feels reduced	52.63	31.58	15.79	73.68*	7.89	18.42
Q2. My joint stiffness feels reduced	47.37	34.21	18.42	78.95*	2.63	18.42
Q3. My morning joint stiffness feels reduced	44.74	26.32	28.95	76.32*	5.26	18.42
Q4. My joint swelling appears reduced	42.86	31.43	25.71	68.57*	8.57	22.86
Q5. My mobility feels improved	47.37	36.84	15.79	76.32*	5.26	18.42
Q6. My joint pain while sitting feels improved	55.26	26.32	18.42	76.32*	2.63	21.05
Q7. My joint pain while lying down feels improved	52.63	28.95	18.42	65.79	15.79	18.42
Q8. I find it easier to fall asleep	42.11	42.11	15.79	65.79	18.42	15.79
Q9. I find it easier to stay asleep	44.74	36.84	18.42	60.53	23.68	15.79
Q10. I no longer wake up too early	36.84	47.37	15.79	60.53	13.16	26.32
Q11. My sleep quality feels improved	47.37	34.21	18.42	60.53	23.68	15.79
Q12. I find it easier to function during day-to day tasks	55.26	28.95	15.79	78.95*	5.26	15.79

Q13. My neuropathic pain feels reduced	55.26	21.05	23.68	77.78*	5.56	16.67

In accordance with the study's specific focus, the parameters related to OA, such as joint pain, joint stiffness, and joint swelling, as well as parameters associated with insomnia and NP, such as convenience in falling asleep, quality of sleep, and neuropathic pain levels, for all 112 subjects, are visually depicted for analysis (figures 1 to 6). Similarly, the evaluation of the set parameters is graphically represented for group 1, group 2 and group 3 patients (figure 7; figure 8; figure 9) respectively.

Evolution of Improvement: Questionnaire Results Across 13 Weeks

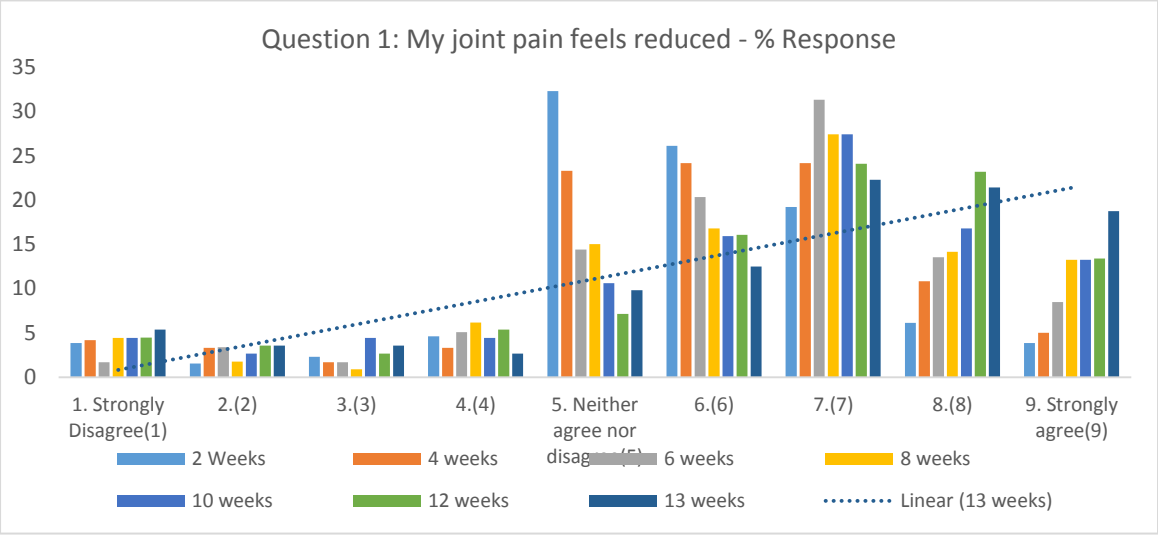

Figure 1: Represents the progression of improvement in joint pain over time

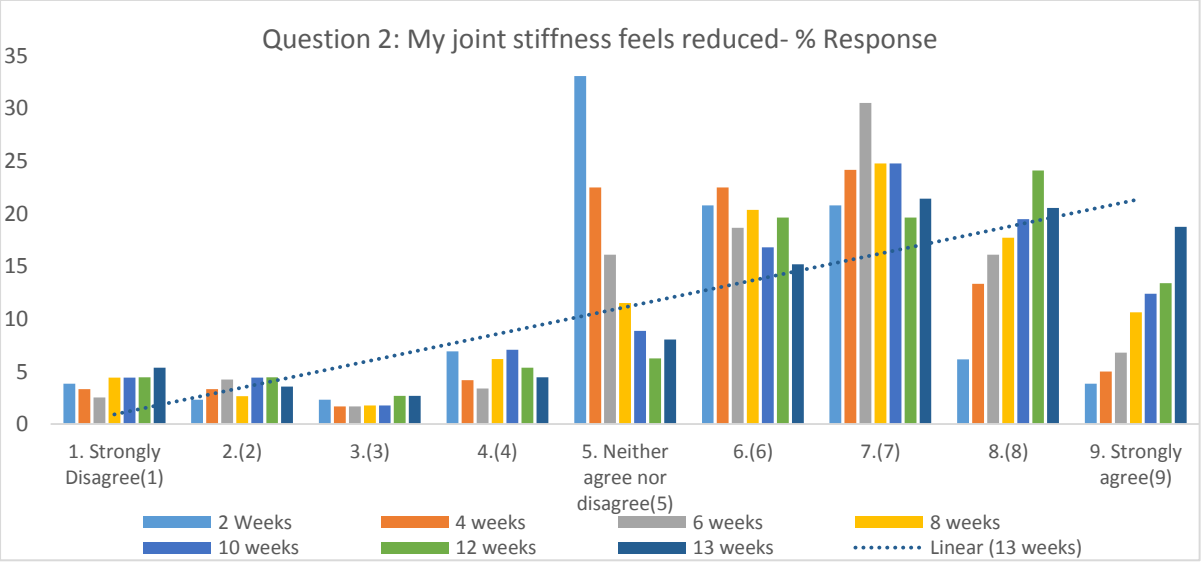

Figure 2: Represents the improvement trends in joint stiffness from week 2- week 13

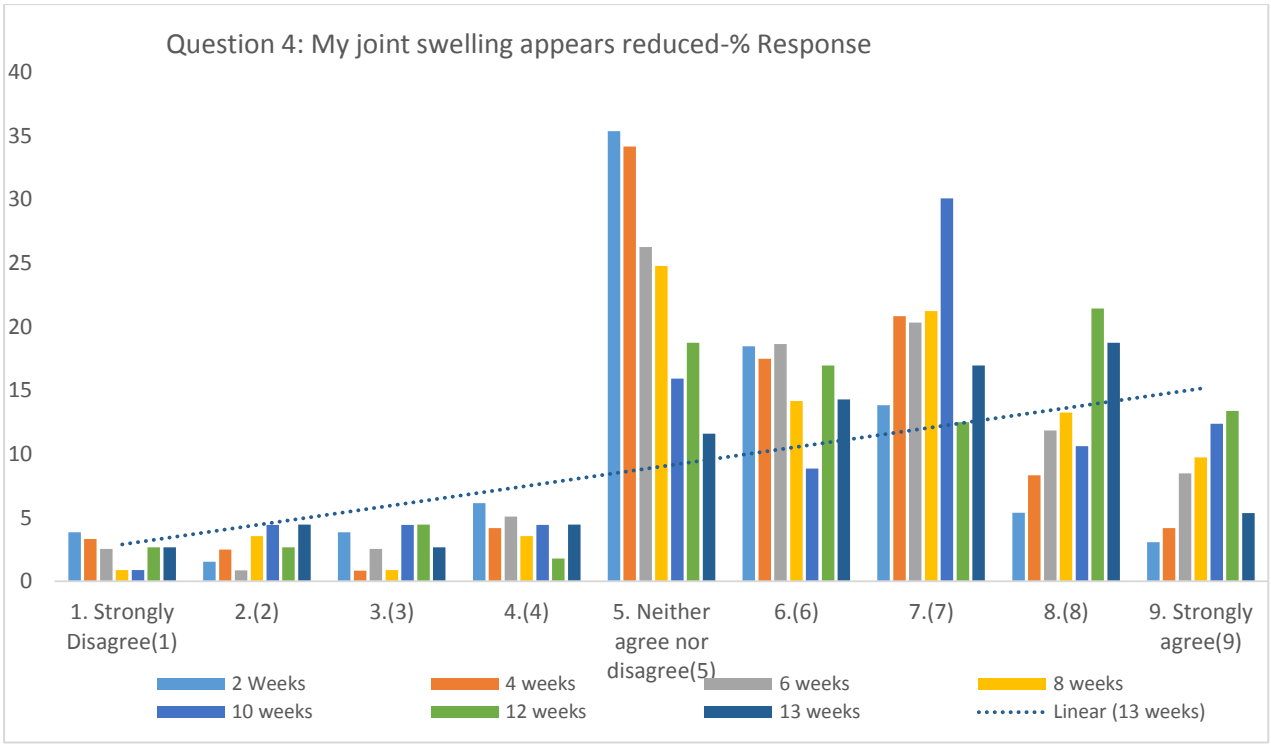

Figure 3: Represents the improvement trends in joint swelling from week 2- week 13

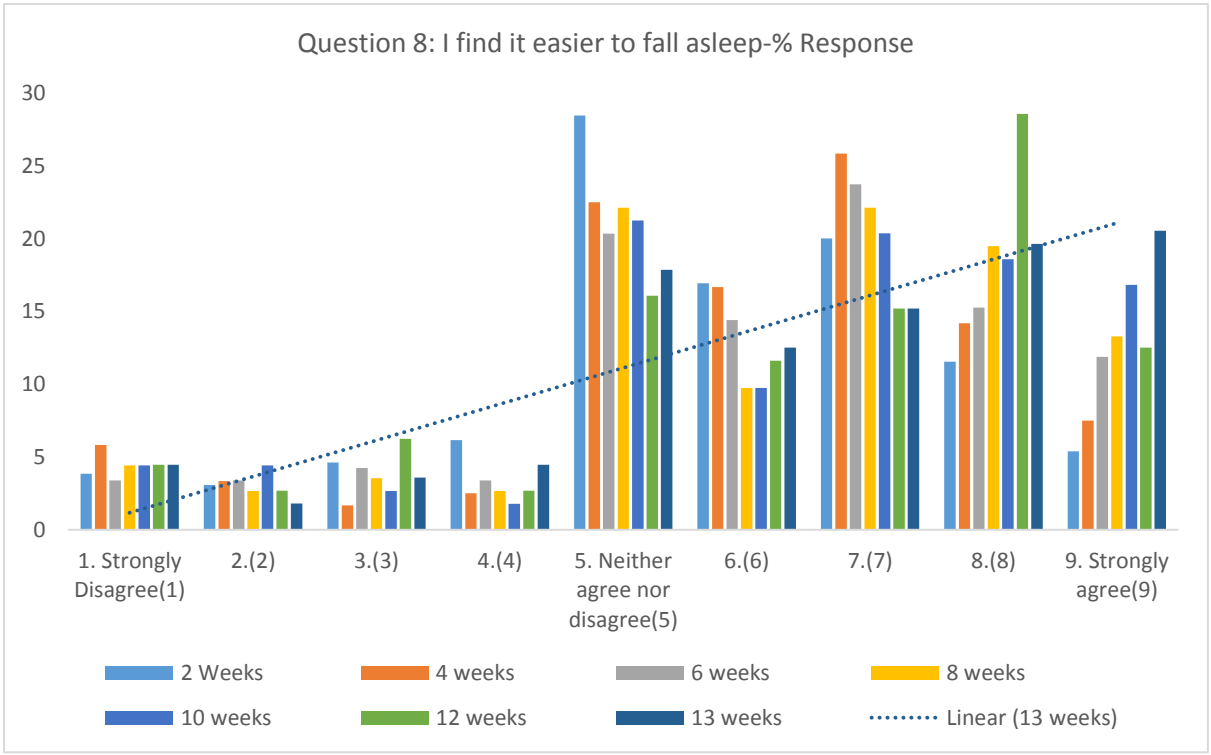

Figure 4: Represents the improvement trends in falling asleep from week 2- week 13

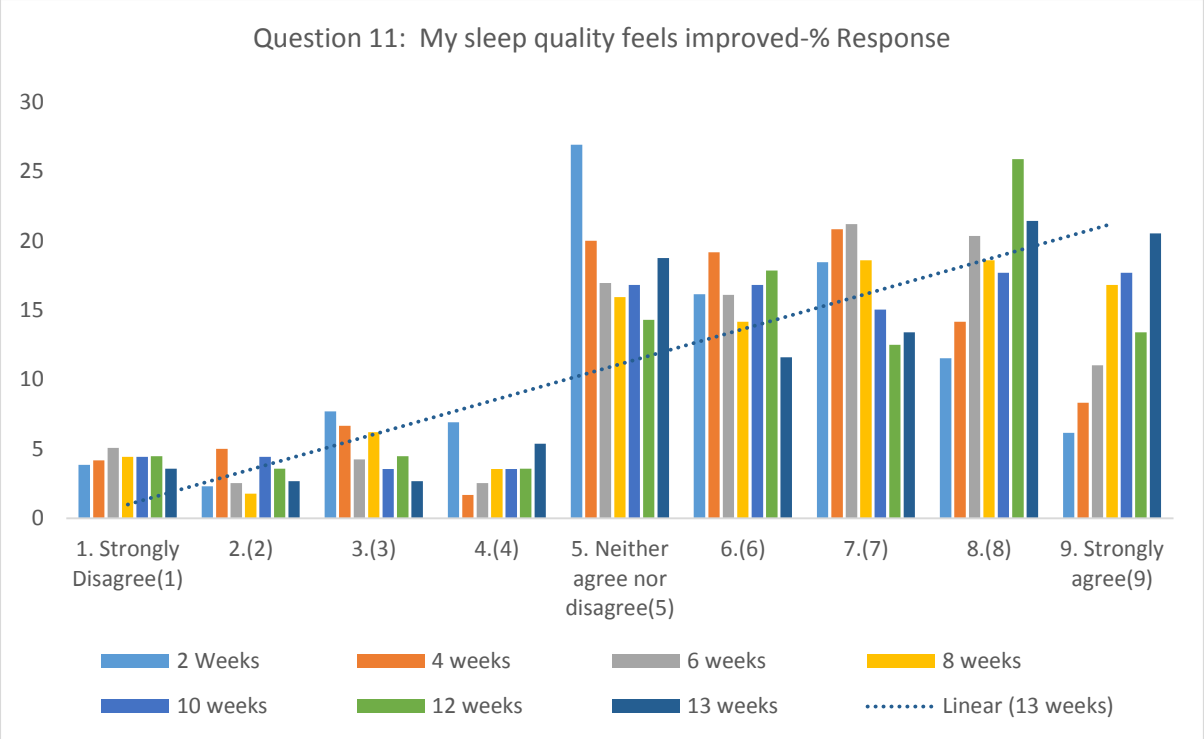

Figure 5: Represents the progression of improvement in sleeping quality over time

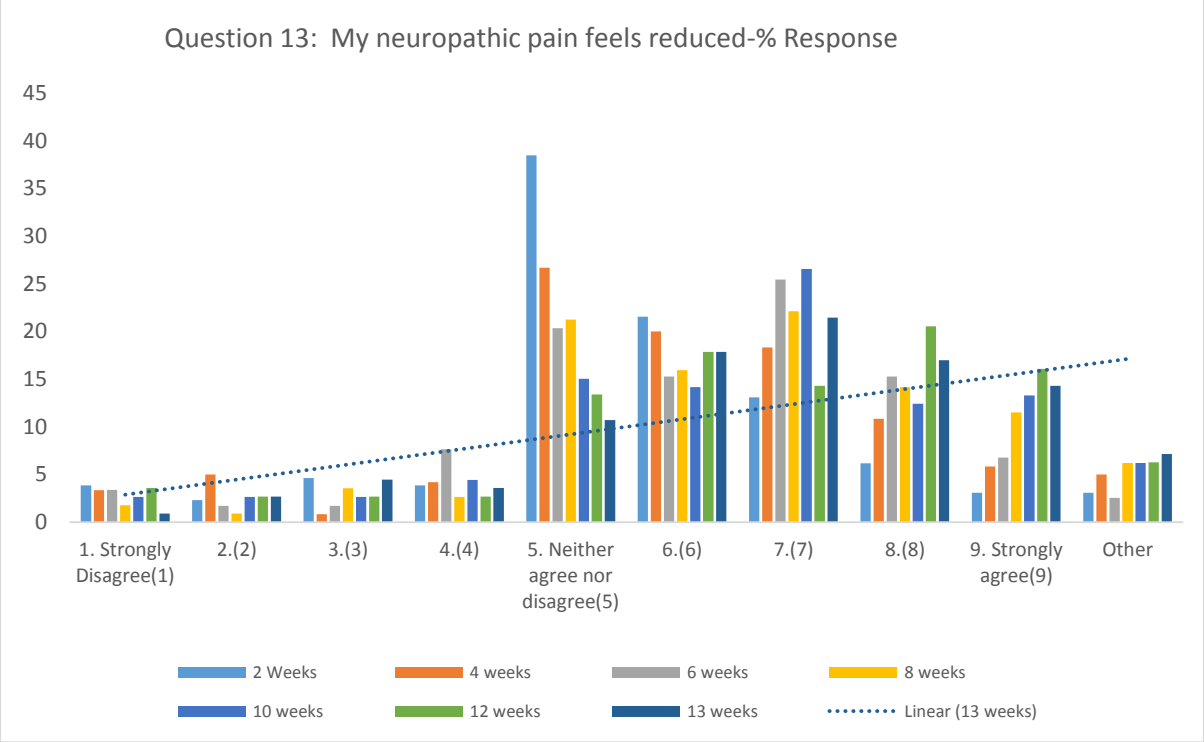

Figure 6: Represents the progression of improvement in neuropathic pain over time

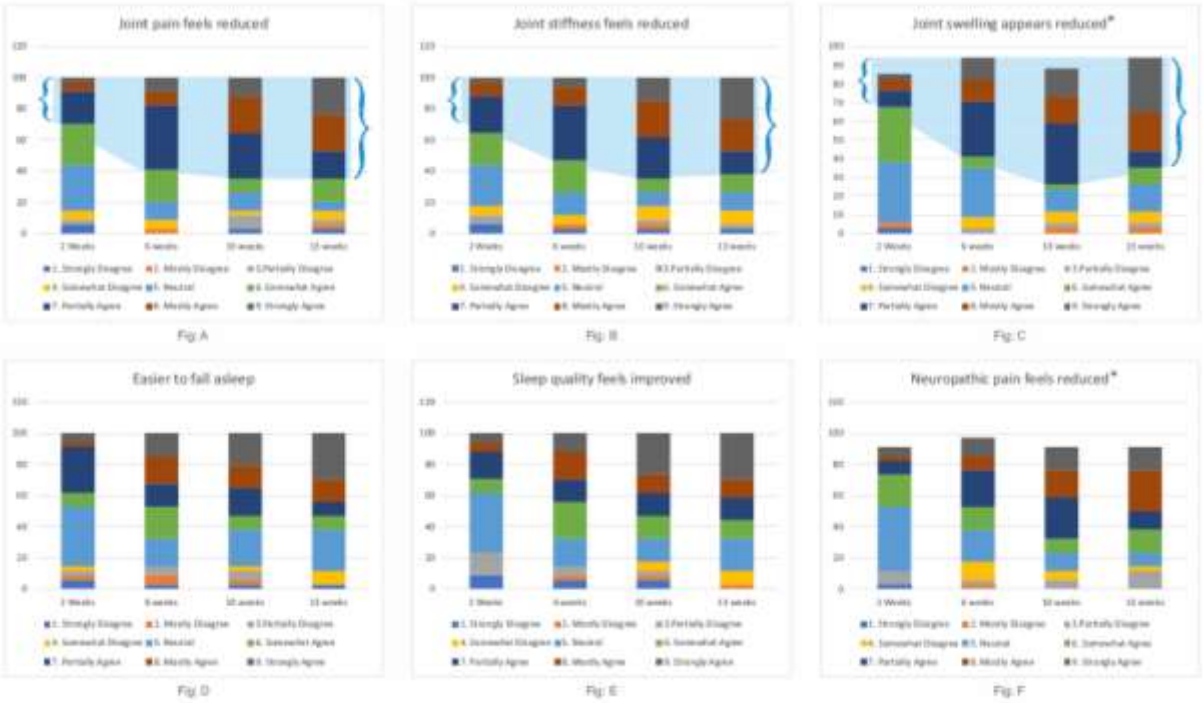

Figure 7: Changes in group 1 patients (OA + HT, n=34); Figure A - reduction in joint pains; Figure B - reduction in joint stiffness; Figure C - reduction in joint swelling; Figure D - improvement in falling asleep; Figure E - improvement in sleep quality; Figure F - reduction in neuropathic pain.

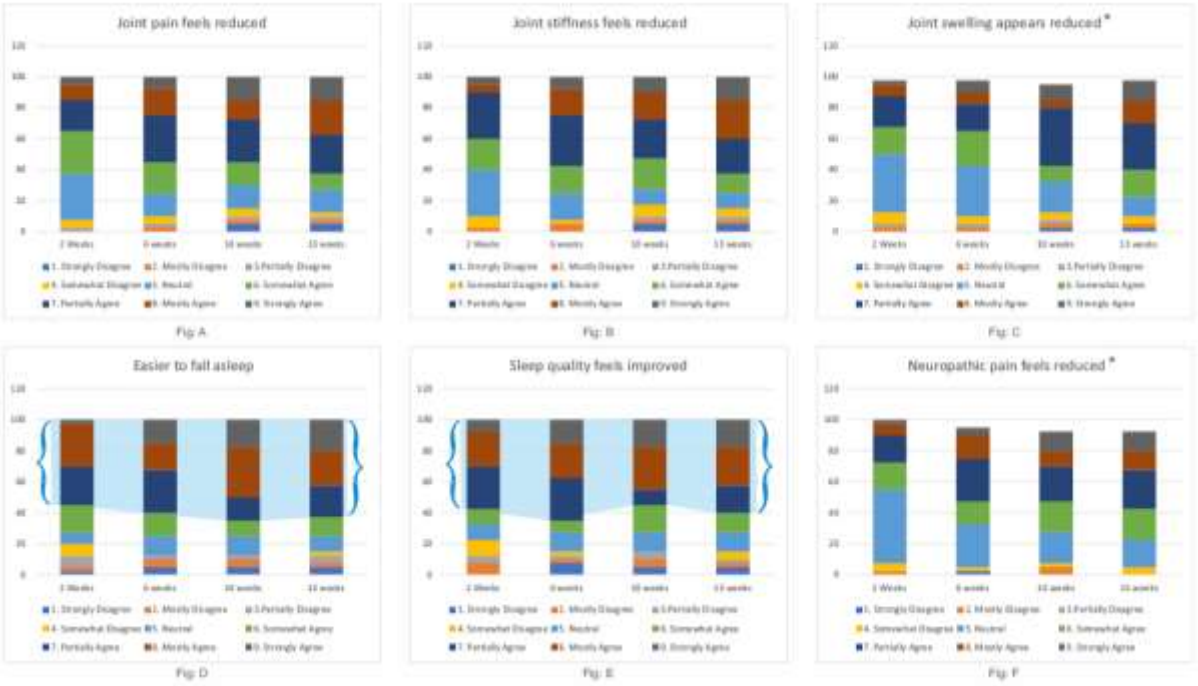

Figure 8: Changes in group 2 patients (OA + insomnia, n=40); Figure A - reduction in joint pains; Figure B - reduction in joint stiffness; Figure C – reduction in joint swelling; Figure D - improvement in falling asleep; Figure E - improvement in sleep quality; Figure F - reduction in neuropathic pain.

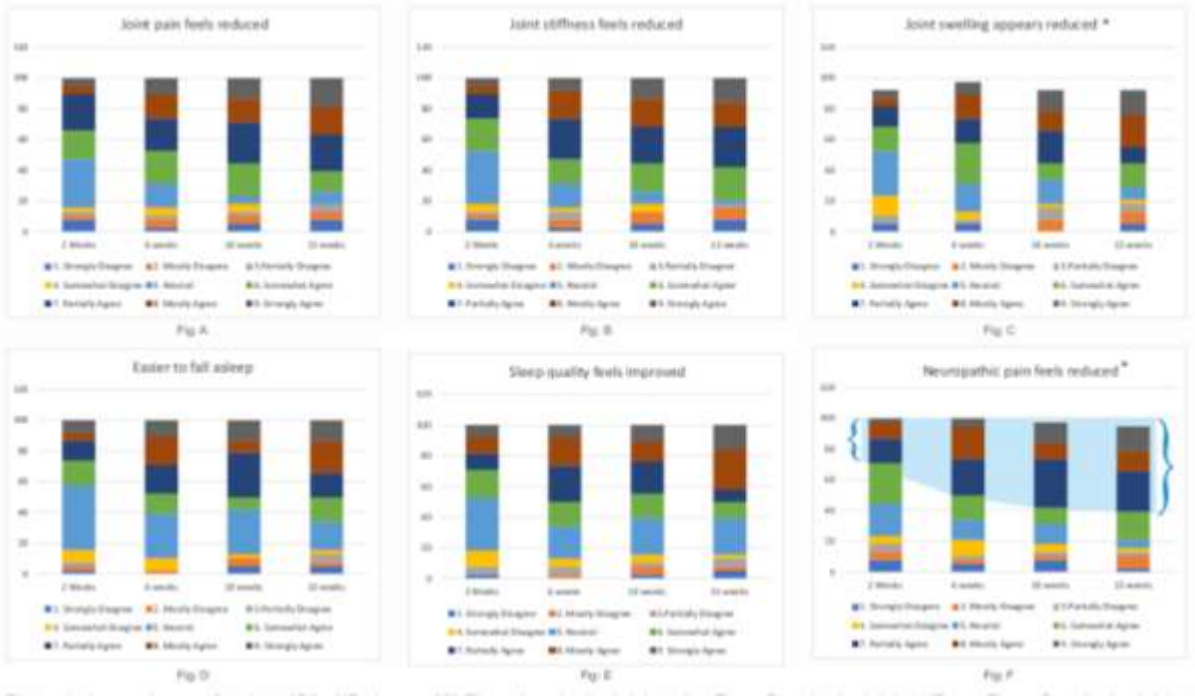

Figure 9: Changes in group 3 patients (OA + NP, n=38); Figure A - reduction in joint pains; Figure B - reduction in joint stiffness; Figure C - reduction in joint swelling; Figure D - improvement in falling asleep; Figure E - improvement in sleep quality; Figure F - reduction in neuropathic pain.

The changes in mean of the responses of all subjects (n=112) from first follow-up (2 weeks) to final week (13 weeks) are tabulated in table 5. Moreover, when patients were asked if they would recommend the product to family and friends, the mean value was high (6.67±2.36), indicating a positive response.

Table 6: Mean and standard deviation (SD) at 2 weeks and at 13 weeks.

	1st follow-up (2 weeks)		**Final (13 weeks)**	
Question	**Mean**	**SD**	**Mean**	**SD**
Question 1: My joint pain feels reduced	5.69	1.62	6.54	2.23
Question 2: My joint stiffness feels reduced	5.62	1.68	6.53	2.21
Question 3: My morning joint stiffness feels reduced	5.6	1.74	6.44	2.19
Question 4: My joint swelling appears reduced	5.45	1.66	6.54	2.13
Question 5: My mobility feels improved	5.71	1.75	6.65	2.15
Question 6: My joint pain while sitting feels improved	5.63	1.73	6.56	2.22
Question 7: My joint pain whilst lying down	5.42	1.8	6.53	2.22

feels improved				
Question 8: I find it easier to fall asleep	5.73	1.87	6.49	2.16
Question 9: I find it easier to stay asleep	5.58	1.92	6.37	2.07
Question 10: I no longer wake up too early	5.35	1.9	6.2	2.03
Question 11: My sleep quality feels improved	5.68	1.92	6.52	2.14
Question 12: I find it easier to function during day-to-day tasks	5.72	1.68	6.59	2.09
Question 13: My neuropathic pain feels reduced	5.44	1.66	6.56	1.86

These findings suggest that XtraBos™ treatment over the 13-week period resulted in significant improvements in joint pain, stiffness, swelling, mobility, sleep quality, and overall functioning in individuals with OA. Additionally, the high recommendation score indicates a favourable perception of the product's effectiveness. These findings underscore the potential effectiveness of XtraBos™ in alleviating neuropathic pain, managing insomnia, and improving joint symptoms in individuals with OA. It could be due to its positive role in both OA & comorbidities.

4. Discussion

The findings of this study demonstrate the potential effectiveness of XtraBos™ in alleviating symptoms and improving overall well-being in individuals with OA and comorbidities. The study assessed the impact of XtraBos™ treatment on various parameters including joint pain, stiffness, swelling, mobility, sleep quality, and others, in patients with comorbidities like HT, sleep disturbances and NP. 112 subjects were considered for the assessment of the results. The results indicated that after 13 weeks of XtraBos™ treatment, patients reported a significant reduction in joint complaints, sleep disturbances and NP. This improvement was reflected in the mean scores obtained for these parameters, which showed a substantial increase from 2 weeks after the treatment (table 6). Table 2 showed the distribution of the scores as per the percentage in 2 weeks and at the end of treatment at 13 weeks. It is observed that all the parameters show an improvement in satisfaction percentage except for the parameter "**I find it easier to stay asleep**" (64.29%) and "**I no longer wake up too early**" (63.39%). Although these two specific parameters did not cross the 'pass mark' but the change from their 2 weeks to 13 weeks treatment showed a drastic progress (53.08% to 64.29%; and 40.77% to 63.39% respectively). The maximum improvement (>20%) was observed for the parameters – **"My joint stiffness feels reduced", "My joint swelling**

appears reduced", "My mobility feels improved", "My joint pain while sitting feels improved", "My joint pain while lying down feels improved", "I no longer wake up too early" and **"My neuropathic pain feels reduced".** The least improvement of all the parameters was observed for the parameter – **"I find it easier to stay asleep"** (11.21%).

For the group 1 patients (OA with HT), the maximum improvement (>20%) was observed in the parameters – **"My joint pain feels reduced"**, **"My mobility feels improved"**, **"My joint pain while sitting feels improved"**, **"I no longer wake up too early"**, **"My sleep quality feels improved"**, **"I find it easier to function during day-to day tasks"**, and "**My neuropathic pain feels reduced".** Neuropathic pains showed drastic reduction (32.25%) in patients of OA with HT. However, the least progress was seen in the parameter – **"My morning joint stiffness feels reduced"** (8.83%)**.**

Considering the group 2 patients (OA with insomnia), the most improvement was observed in the parameters – **"My joint swelling appears reduced"** and "**My neuropathic pain feels reduced"** (30.68%). There were non significant changes observed in the parameter – **"I find it easier to fall asleep"** (2.5%) **"My sleep quality feels improved"** (5%). This can be due to the reason that sleep disturbances are the primary complaint of these patients. Thus, managing pain was comparatively easier in less duration than managing sleep complaints.

The changes observed for group 3 patients (OA with NP), showed improvement (>20%) in almost all the parameters. The highest improvement was seen in the parameters – "**My joint stiffness feels reduced"** and **"My morning joint stiffness feels reduced"** (both 31.58%). However, the least improvement was observed in the parameters – "**My joint pain while lying down feels improved"** and **"My sleep quality feels improved"** (both 13.16%).

6 subjects also reported adverse events in the course of treatment. Among the 6 subjects, 2 reported irritation in abdomen (cramps or diarrhoea), 1 reported irritation in arms and 1 reported nausea. Apart from them, 1 subject reported lethargy. Remaining 1 subject reported low mental state which as per the subject's own description was a usual entity for him in winters. 2 subjects even reported that the repetition of the treatment did not worsen the irritation. Out of the 6 subjects, 4 mentioned using some other product simultaneously with the treatment. Thus, due to the mentioned reasons, it is difficult to establish the direct relatability of the adverse events to the treatment product.

The findings suggest that XtraBos™ has the potential to effectively alleviate pain, and improve joint function in individuals with OA and HT. Moreover, patients reported

improvements in mobility and the ability to perform day-to-day tasks. This suggests that XtraBos™ treatment may enhance functional abilities and overall quality of life in individuals with OA. These positive outcomes are essential for individuals experiencing chronic pain and functional limitations associated with OA, as they can lead to improved physical and psychological well-being. The study also revealed notable improvements in sleep-related outcomes in OA patients with HT & NP. Patients reported easier sleep initiation, better sleep maintenance, and reduced early morning awakenings. Additionally, there was a notable improvement in sleep quality, as indicated by the mean score obtained. Sleep disturbances are common in individuals with OA and can further exacerbate their pain and overall well-being. Remarkable progress was observed in patients of OA with NP who showed improvement in majority of the complaints as compared to other groups. The observed improvements in sleep parameters suggest that XtraBos™ treatment may have a positive impact on sleep quality in individuals OA patients with HT & NP, contributing to better rest and overall recovery. However, patients primarily reporting insomnia as their main concern exhibited minimal shifts in sleep parameters. This outcome might suggest the potential absence of Boswellia serrata's effectiveness in addressing primary insomnia.

The results of this study are consistent with previous researches highlighting the anti-inflammatory, analgesic, cartilage-protective, and antioxidant properties of Boswellia serrata. According to the pilot study, the treatment with Boswellia serrata extract was found to be both safe and effective in alleviating symptoms associated with knee problems in individuals with OA.[30] Meanwhile, XtraBos™'s anti-inflammatory action helps reduce inflammation in the joints affected by OA, thereby alleviating pain, swelling, and stiffness. Additionally, XtraBos™'s analgesic properties contribute to pain relief and improved pain coping mechanisms in individuals with OA. The cartilage-protective effects of AKBA help preserve joint integrity and slow down the progression of joint damage.[31] Furthermore, AKBA's antioxidant properties counteract oxidative stress, reducing further cartilage degradation and inflammation in the joints. A notable limitation of this study is the absence of continuous blood pressure monitoring throughout the entire duration of the research. While baseline and final visit blood pressure measurements were recorded, the lack of ongoing monitoring may have resulted in an incomplete understanding of the potential fluctuations or trends in patients' blood pressure levels during the study period. This limitation could impact the comprehensive assessment of the relationship between osteoarthritis symptoms and blood

pressure changes, potentially leading to an underrepresentation of the impact of hypertension on the study outcomes.

Although the findings of this study are promising, further research is warranted to determine optimal dosage, long-term safety, and potential synergistic effects of XtraBos™ with other treatments. Additionally, investigating the efficacy of XtraBos™ in a larger and more diverse population for a longer duration would provide a more comprehensive understanding of its potential benefits. The findings also suggest that XtraBos™ holds promise as a potential therapeutic option for individuals with OA and comorbidities, including HT. The significant improvements in joint pain, stiffness, swelling, mobility, sleep quality, and neuropathic pain indicate the potential of XtraBos™ in enhancing symptom control and overall well-being. Further exploration and research into XtraBos™'s efficacy, safety, and long-term effects through in-vitro studies and control trials, are necessary to establish it as a valuable treatment option for individuals with OA and its associated comorbidities.

5. Conclusion

The intriguing potential of XtraBos™ as a therapeutic alternative has a positive effect on people with OA and related comorbidities. Patients saw significant reductions in joint pain, sleep disturbances, and NP during the course of the 13-week study. The extraordinary effects of XtraBos™ may be linked to the special qualities of its extract. AKBA efficiently lessens joint discomfort and improves mobility by lowering inflammation and focusing on pain pathways. Additionally, its antioxidant qualities mitigate oxidative stress, shielding cartilage from further damage. This multifaceted strategy helps people with OA feel better in a complete way. Furthermore, the effects of XtraBos™ go beyond symptoms. Patients reported higher-quality sleep, improvement in neuropathic pains, which allowed for greater rest and recuperation. This is essential since nerve pains and sleep disruptions often worsen joint complaints and negatively influence general wellbeing. By addressing this issue, XtraBos™ provides a comprehensive strategy for enhancing the lives of people with OA. By investigating the therapeutic potential of natural substances like Boswellia serrata extract, we open the door for cutting-edge OA treatment strategies, eventually providing hope and better results for patients suffering from this chronic illness. Nevertheless, the implementation of in-vitro studies and randomized controlled trials in near future, holds significant promise in providing a comprehensive evaluation of the mode of action, potentially informing personalized treatment modalities, and optimizing strategies for the management of OA.

6. References

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