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Effectiveness and Safety of Devil's Claw Tablets in Patients with General Rheumatic Disorders

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Arthritis and other rheumatic conditions (AORC) are the leading cause of disability, are associated with poor quality of life and incur considerable direct and indirect costs. It is considered that the instance of AORC will continue to increase. To assess the effectiveness, safety and tolerability of Harpagophytum (Bioforce) in the treatment of AORC, a single group open study of 8 weeks duration (259 patients) was performed in the United Kingdom. Effectiveness was assessed by numeric rating scales, the Western Ontario and McMasters Universities Osteoarthritis (WOMAC) Index and the Algofunctional Hand Osteoarthritis Index. Tolerance was measured by a numeric rating scale and safety by self-reporting, blood analysis and liver function tests. Quality of life was measured by SF-12 questionnaire. There were statistically significant ($p < 0.0001$) improvements in patient assessment of global pain, stiffness and function. There were also statistically significant reductions in mean pain scores for hand, wrist, elbow, shoulder, hip, knee and back pain. Quality of life measurements (SF-12) were significantly increased from baseline and 60% patients either reduced or stopped concomitant pain medication. Harpagophytum is an effective and well-tolerated serious treatment option for mild to moderate degenerative rheumatic disorders providing improved quality of life measure. Copyright © 2007 John Wiley & Sons, Ltd.

Keywords: Devil's Claw; Harpagophytum; joint pain; general rheumatic disorders.

INTRODUCTION

World-wide, arthritis and other rheumatic conditions (AORC) are the leading cause of disability. Compared with any other chronic disease, musculoskeletal disorders are associated with poorer results in quality of life measurements (Reginster, 2002). In addition, the direct and indirect costs are considerable. In developed countries these costs are substantial (Huscher *et al.*, 2006; Hallert *et al.*, 2006; Yelin *et al.*, 1986). In developing countries a considerable proportion of patients' annual average income is consumed by AORC (Osiri *et al.*, 2007). The instance of AORC is expected to increase substantially by 2030, resulting in a large impact on patient wellbeing and a high economic burden to society (Hootman and Helmick, 2006; Woolf and Akesson, 2001). The current movement in healthcare in the 21st century is centred on patient empowerment and education (Baker, 2000) and as such it is vital that a wealth of reliable material exists to enable informed patient choice.

Conventional pharmaceutical treatments for general rheumatic disorders generally consist of non-steroidal antiinflammatory drugs (NSAIDs). NSAIDs act mainly on prostaglandin pathways. Given the side effects observed with NSAID use, there is a growing trend towards the use of phytotherapeutic remedies. However, rigorous evaluation of their effectiveness and safety in many instances remain to be elucidated. The use of phytotherapeutic remedies may be associated with potential risks. The active ingredients in herbal therapies or drugs may produce herb/herb or herb/drugs interactions that have undesirable or potential damaging side effects.

Harpagophytum procumbens (Hp), commonly known as Devil's Claw, is a perennial plant which thrives in arid conditions in Southern Africa. For centuries, it has been used as a traditional treatment for a variety of illnesses. It was introduced to Europe in the early twentieth century and is widely recommended by herbalists as a popular antiinflammatory and analgesic preparation for musculoskeletal disorders. The efficacy of *Hp* in the relief of arthritic symptoms has been investigated in numerous animal, clinical and *in vitro* studies (Grant *et al.*, 2007).

Although the active principle of *Hp* has yet to be elucidated, the pharmacologically active components of the root tubers of *Hp* are considered to be the iridoid glycosides which comprise approximately 3% of the total plant material (Baghdikian *et al.*, 1997). Additional constituents include carbohydrates (stachyose, raffinose, monosaccharides), flavonoids (kaempferol, luteolin), aromatic acids (caffeic acid, chlorogenic acid, cinnamic acid), phytosterols, (β-sitosterol, stigomasterol), triterpenes (ursolic and oleanic acid), 2-phenyl-ethyl derivatives (acteoside, isoacteoside) and harpagoquinone (Burger *et al.*, 1987). The European Scientific Cooperative on Phytotherapy ESCOP-monograph for

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Harpagophyti radix recommends 2–5 g of the drug or equivalent aqueos or hydroalcoholic extracts for the treatment of painful osteoarthritis. However, the cut and dried secondary root tubers of Devil's Claw yield a variety of other compounds which are considered biologically active and some studies (e.g. Wegener, 2000) report that kaempferol directly inhibits cyclooxygenase-2.

A substantial number of clinical trials exist with the aim of determining the effectiveness and safety of *Hp* preparations in the treatment of various forms of musculoskeletal pain (Grant *et al.*, 2007). However, due to the heterogeneity of these studies in terms of trial design, treatment dose, extraction methods used and the clinical conditions monitored, direct comparisons and the quantitative evaluation of outcome measures are not feasible. This study was designed specifically to investigate the effectiveness and safety of *Hp* tablets in the treatment of patients with general rheumatic disorders, monitoring a variety of biochemical and clinical parameters. Although other open studies have been carried out using aqueous *Hp* (Grahame and Robinson, 1981; Laudahn and Walper, 2001; Wegener and Lupke, 2003) none has looked at the influence of *Hp* on different joints, measured tolerance and safety parameters and assessed patient satisfaction.

MATERIALS AND METHODS

The study presented was a single group open study of 8 weeks duration, performed in the United Kingdom between May 2003 and December 2004. The study was conducted in accordance with ICH-Good Clinical Practice Guidelines, the Declaration of Helsinki, and the local laws and regulations. The study protocol was reviewed and approved prior to commencement of the study by the Bioforce (UK) Ltd Independent Research Ethics Committee (BIREC).

Patient inclusion criteria. Ambulatory patients (age 18–75 years) were recruited into the study having given their written informed consent. Patients who were included reported mild to moderate rheumatic disorder in at least one joint or body area, and had experienced pain (rated 2–7 on a 10 point scale) in the affected joint/body area on at least 2 days per week during the previous 8 weeks.

Patient exclusion criteria. Patients were excluded from the study if they suffered from diabetes, gastric or duodenal ulcers, gallstones, or were allergic to Pedaliaceae (Harpagophytum and related plants). Those with current symptoms or a history of secondary osteoarthritis (e.g. acromegaly, gout), or any other severe illness (e.g. malignant tumours, cardiac, renal or hepatic diseases) were also excluded. Patients undergoing physiotherapy or similar physical treatments (e.g. acupuncture) of the affected body area less than 4 weeks before the beginning of the study were excluded. Those given intra-articular corticosteroid therapy less than 8 weeks before the beginning of the study, or scheduled to have a joint replacement during the study were also excluded.

Patients regularly taking H2 antagonists, proton pump inhibitors, other indigestion remedies, or homeopathic products indicated for treating general rheumatic disorders (e.g. Rhus Tox, Arnica) were excluded. Those commencing treatment with new analgesics, NSAIDs, or any herbal product indicated for treating general rheumatic disorders less than 2 weeks before the beginning of the study were excluded. Patients starting food supplements indicated for treating general rheumatic disorders less than 8 weeks before the beginning of the study were also excluded.

Study procedure. Study visits were planned at day 0 (baseline), week 4 and week 8 (study endpoint). Harpagophytum tablets (Devil's Claw tincture tablets/ A. Vogel Rheuma Tabletten containing 480 mg dry extract, DER 1.5-3:1, extractant : 60% ethanol v/v) were dispensed to all patients at day 0 and week 4. The total daily intake of Harpagophytum dry extract was 960 mg for each patient. These tablets were to be taken orally at a daily dosage of 2 tablets (morning and evening with food) for 8 consecutive weeks. Pre- (visit 1) and post- (visit 3) treatment blood samples for full blood count (FBC) and liver function test (LFT) analysis were taken from a subgroup of 35 patients.

Effectiveness. The following methods were used to assess the effectiveness of treatment with Harpagophytum tablets:

Global assessment. Global assessment of pain, function and stiffness in the affected area during the previous 24 h was made on a numeric rating scale (NRS). All patients completed an NRS at each study visit, and possible scores ranged from 0 (no pain) to 10 (worst possible pain).

Specific assessment. Joint specific general rheumatic disorders were also assessed according to which affected joints the patients presented with at baseline. Patients experiencing pain associated with general rheumatic disorders in the hand, wrist, elbow, shoulder, hip, knee, back or soft tissues at baseline completed an NRS at each study visit. Possible scores for the NRS ranged from 0 to 10 as above.

The Western Ontario and McMasters Universities Osteoarthritis (WOMAC) Index (Bellamy, 2000) was used to assess knee and hip joints affected by general rheumatic disorders at baseline. Thereafter, the index was calculated at each study visit. The WOMAC Index was used to calculate three subscale scores for pain, stiffness and function of the affected joint. A WOMAC Index total subscale score was calculated from the unweighted mean of the three normalized subscale scores (sum of scores normalized from 0 to 10).

Functional assessment. The Algofunctional Hand Osteoarthritis Index (Dreiser *et al.*, 1995) used 10 questions to assess the functional ability of a patients dominant hand affected by a general rheumatic disorder at baseline. Thereafter, the index was calculated at each study visit. Possible scores for function were 0 (without difficulty), 1 (with slight difficulty), 2 (with great difficulty) and 3 (impossible).

Finger floor distance (in cm) was measured at baseline and at earch study visit for patients with back pain.

Perceived effectiveness. A general assessment of effectiveness was made at week 8 using a 6-point scale.

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Patients rated the effectiveness of their treatment as being 'excellent', 'good', 'moderate', 'no change', 'unsatisfactory', or 'poor'. The primary investigator also reported his perceived effectiveness of treatment for each patient using the same scale.

The onset of action of the treatment was assessed at week 4, by asking patients if and when they felt a benefit. Those reporting no benefit were asked the same question at week 8.

Patients completed a daily diary in which they rated levels of pain, stiffness and difficulty experienced. Diaries issued at baseline were returned to the investigator at week 4, and those issued at week 4 were returned at week 8. These diaries were also used to help monitor compliance with treatment.

A Quality of Life Questionnaire (SF-12) was used to assess the physical and emotional status of each patient during the study (Ware *et al.*, 1996). The SF-12 was completed at each study visit.

In an attempt to obtain a further insight into the patient's use of pain and antiinflammatory medication, a daily diary was completed by the patient. This diary also acted as a helpful tool to assess compliance.

Compliance with treatment. Patients returned unused medication at week 4 and week 8 in order to count the remaining tablets. Compliance with treatment was determined from tablet counts made for each patient.

Safety and tolerability. At each visit, patients were asked non-leading questions about their well-being. All adverse events encountered during the study were reported, whether considered to be related to study medication or not. The patients were informed that an adverse event was any change from their baseline (pre-treatment) condition, other than improvement. All adverse events were followed up to resolution. Patients were also asked if they had experienced any gastric problems. The patients were also informed that should any serious adverse events occur during the course of the study they must be reported to the Medical Director of Bioforce as soon as possible. The ICH GCP (1996) Guidelines formed the basis of the working definition of a serious adverse event.

A serious adverse event was defined as any untoward medical event that at any dose:

- Resulted in death
- Was life threatening (i.e. subject is at immediate hazard)
- Required inpatient hospitalization or prolongation of existing hospitalization
- Resulted in persistent or significant disability/incapacity, or
- Was a congenital anomaly/birth defect.
- Required intervention to prevent one of the above

Tolerability of treatment was assessed at week 8 using a 3-point scale. Patients rated their tolerability as being 'good', 'average', or 'poor'. The primary investigator also reported his perceived tolerability for each patient using the same scale for comparison.

Overall acceptance of treatment was assessed by asking each patient if they would consider using Harpagophytum again. A 'yes', 'no' or 'possibly' answer was elicited.

Statistical analyses. Effectiveness assessments were performed on data from patients in the intention to treat population (ITT). Patients included in the ITT population had taken at least one Harpagophytum tablet and attended a study visit at baseline and at least one post-baseline visit. Compliance with treatment was also assessed using data for the ITT population.

Safety and tolerability assessments were performed on data from patients in the safety population who had taken at least one Harpagophytum tablet. Data were presented as mean (± standard deviation) unless otherwise stated. Changes from baseline to week 4, and to week 8, with respect to global assessment scores for pain, stiffness and function, joint specific pain scores, WOMAC Index scores, Algofunctional Hand Osteoarthritis Index scores, SF-12 subscale scores, patient diary scores for pain, stiffness and difficulty, and clinical laboratory evaluations, were analysed using the Wilcoxon signed rank test with significance set at the 5% written informed consent level.

RESULTS

Patient demographics

A total of 259 patients (safety population) were treated with Harpagophytum. Of these, 222 patients (Intention To Treat [ITT] population) were included in the effectiveness assessments. The majority of the patients presented with a history (greater than 5 years) of rheumatic conditions. The baseline demographic characteristics of the patient group are shown in Table 1.

Compliance with treatment

Compliance with treatment measured by tablet count was 75–100% for 140 patients (63.1%) at week 8 (Table 7).

The study had a high completion rate (81.1%), with only 11 patients (4.2%) discontinuing treatment due to adverse events. The remaining 26 patients discontinued treatment due to withdrawal of consent (9.3%), were lost to follow up (4.6%), or due to a protocol violation (0.8%).

Table 1. Demographic characteristics of patients at baseline

Demographic characteristic	ITT population (n = 222)	Safety population (n = 259)
Gender		
Male	82 (36.9%)	95 (36.7%)
Female	140 (63.1%)	164 (63.3%)
Age (years)		
All		
Mean	56.6 ± 10.2	56.2 ± 10.5
Range	23.0–75.0	19.0–75.0
Male n	82	95
Mean	57.1 ± 9.4	56.3 ± 10.4
Range	35.0–75.0	19.0–75.0
Female n	140	164
Mean	56.3 ± 10.6	56.1 ± 10.6
Range	51.0–64.0	23.0–74.0

Mean data expressed as mean ± standard deviation.

Table 2. Global assessments of pain, stiffness and function (numeric rating scale from 0 to 10). Data for the ITT population

Assessment	Visit 1	Visit 2	Visit 3
Global pain	4.9 ± 2.1	3.7 ± 2.0[a]	3.3 ± 2.2[a]
Global stiffness	5.1 ± 2.3	3.6 ± 2.2[a]	3.1 ± 2.2[a]
Global function	3.5 ± 2.5	2.4 ± 2.3[a]	2.1 ± 2.3[a]

All data presented as mean ± standard deviation (n = 207).
[a] $p < 0.0001$ (Wilcoxon Test; compared with corresponding Visit 1 score).

Effectiveness

Global assessments of pain, stiffness and function were performed on data available for 207 patients (Table 2). Global mean scores for pain, stiffness and function were significantly reduced from baseline to week 4 and week 8 ($p < 0.0001$).

Mean scores for pain in the hand, wrist, elbow, shoulder, hip, knee and back were significantly reduced from baseline to week 8 ($p < 0.05$). These mean scores for pain (except for right elbow) were also significantly reduced from baseline to week 4 ($p < 0.01$). Mean scores for pain in soft tissues were reduced from baseline (6.0 ± 1.0) to week 8 (3.7 ± 3.1). However, data were only available for three patients and these differences were not significant.

The WOMAC Index subscale mean scores were available for 114 and 68 patients with general rheumatic disorders of the knee and hip joints, respectively (Tables 3 and 4). All subscale mean scores were significantly reduced from baseline to week 4 and week 8 ($p < 0.0001$). Mean scores for the Algofunctional Hand Osteoarthritis Index were available for 113 patients and were significantly reduced from baseline (6.5 ± 5.1) to week 8 (4.5 ± 4.7) ($p < 0.0001$). Finger floor distances were available for 81 patients who presented with back pain at baseline. Mean distances were significantly reduced from baseline (18.3 ± 15.0 cm) to week 8 (12.9 ± 12.7 cm) ($p < 0.0001$).

Table 3. WOMAC Index for patients with a general rheumatic disorder of the knee. Data for the ITT population (patients with complete data at all visits)

Subscale	Visit 1	Visit 2	Visit 3
Pain (n = 114)	4.2 ± 1.6	2.9 ± 1.8[a]	2.7 ± 1.9[a]
Stiffness (n = 115)	5.4 ± 1.8	3.9 ± 1.9[a]	3.5 ± 2.1[a]
Function (n = 115)	4.2 ± 1.8	3.1 ± 1.8[a]	2.7 ± 1.8[a]
Total (n = 116)	4.6 ± 1.5	3.3 ± 1.7[a]	2.9 ± 1.8[a]

All data presented as mean ± standard deviation.
Figures in parentheses indicate n value.
[a] $p < 0.0001$ (Wilcoxon Test; compared with corresponding Visit 1 score).

Table 4. WOMAC Index for patients with a general rheumatic disorder of the hip. Data for the ITT population (patients with complete data at all visits)

Subscale	Visit 1	Visit 2	Visit 3
Pain	4.2 ± 1.8	3.0 ± 1.7[a]	2.6 ± 1.9[a]
Stiffness	5.3 ± 1.6	4.1 ± 1.9[a]	3.4 ± 2.0[a]
Function	4.0 ± 1.8	3.0 ± 1.8[a]	2.4 ± 1.8[a]
Total	4.5 ± 1	3.3 ± 1.7[a]	2.8 ± 1.8[a]

All data presented as mean ± standard deviation (n = 68).
[a] $p < 0.0001$ (Wilcoxon Test; compared with corresponding Visit 1 score).

Table 5. Global assessment of effectiveness for the ITT population

Effectiveness	Assessment by patient	Assessment by investigator
Excellent	52 (23.4%)	52 (23.4%)
Good	68 (30.6%)	66 (29.7%)
Moderate	43 (19.4%)	47 (21.2%)
No change	47 (21.2%)	45 (20.3%)
Not applicable	12 (5.4%)	12 (5.4%)

General assessments of effectiveness made by each patient and the investigator are shown in Table 5. Effectiveness was rated as being excellent or good by 120 patients (54.1%). Investigators perceived effectiveness to be excellent or good in 118 patients (53.2%).

A total of 171 patients (77.0%) in the ITT population reported feeling a beneficial effect from using Harpagophytum tablets. One hundred and four of these patients noticed an effect between 1 and 4 weeks after baseline. Mean scores for pain, daily functions and stiffness were calculated from patient diaries. All mean scores were significantly reduced from week 1 to week 2 and week 8 ($p < 0.0001$). The SF-12 mean scores for physical and emotional subscales were available for 207 patients. Mean scores for both subscales were significantly increased from baseline to week 4 and week 8 ($p < 0.0001$) (Table 6).

Clinical laboratory evaluation

For a subpopulation of 35 patients blood samples were taken for FBC and LFT analysis pre- (visit 1) and post- (visit 3) treatment. The results of patients in the ITT population who had complete datasets at all visits were analysed and these are presented in Table 7. With the exception of one parameter, there were no significant changes in the blood parameters measured and all values were within the normal range at both visit 1 and 3. AST values were above the normal range at visit 1 and despite decreasing significantly ($p < 0.05$) at visit 3, they remained above the normal range.

Concomitant medication

Concomitant medication was being taken by 243 patients (93.8%) in the safety population at baseline. Analgesics

Table 6. Quality of life (SF-12) for the ITT population (patients with complete data at all visits)

Subscale	Visit 1	Visit 2	Visit 3
Physical	42.0 ± 9.4	45.1 ± 8.9[a]	46.2 ± 8.5[a]
Emotional	49.0 ± 10.3	53.3 ± 8.8[a]	54.1 ± 8.1[a]

All data presented as mean ± standard deviation (n = 207).
[a] $p < 0.0001$ (Wilcoxon Test; compared with corresponding Visit 1 score).

Table 7. Compliance with treatment (ITT population)

Compliance	At visit 2	At visit 3
Unknown – compliance not documented	36 (16.2%)	44 (19.8%)
<75%	4 (1.8%)	4 (1.8%)
75–99%	95 (42.8%)	99 (44.6%)
100%	51 (23.0%)	41 (18.5%)
101–120%	34 (15.3%)	32 (14.4%)
>120%	2 (0.9%)	2 (0.9%)

n = 222.

specifically for general rheumatic disorders were taken by 154 patients in the ITT-population (69.3%) at baseline. Of those patients taking analgesics for general rheumatic disorders at baseline, 9.1% increased their dosage, 16.9% had the same dosage and 44.8% decreased their dosage at week 8. In addition, 26.0% had completely stopped taking analgesics for general rheumatic disorders at week 8.

Safety and tolerability

A total of 49 drug-related adverse events (AEs) were reported for 44 patients (17.0%) in the safety population. These AEs were considered to have only a possible/probable relationship to the study medication. No serious AEs were reported, and all were mild to moderate in severity and were in the majority gastrointestinal complaints.

Vital signs and laboratory evaluation of full blood counts and liver function showed no clinically significant changes from baseline in patients (Tables 8 and 9).

Tolerability of treatment was rated 'good' by 194 patients (87.4%). Investigators perceived tolerability to be good in 196 patients (88.3%). Only one patient (0.5%) rated their tolerability as being poor.

When patients were asked if they would use Harpagophytum tablets again, 165 patients (74.3%) answered 'yes', 28 patients (12.6%) answered 'possibly', and only 17 patients (7.7%) answered 'no'.

Table 8. Results of full blood count

Parameter	Baseline	Visit 3
Haemoglobin (g/dL)	14.3 ± 1.2	14.2 ± 1.3
White blood cells ($\times 10^9$/L)	6.2 ± 1.8	6.1 ± 1.8
Platelets ($\times 10^9$/L)	228.0 ± 46.3	229.6 ± 49.2
Red blood cells ($\times 10^{12}$/L)	4.6 ± 0.4	4.5 ± 0.4
Haematocrit (%)	41.6 ± 3.5	41.1 ± 3.4
Mean cell volume (fL)	90.8 ± 3.6	90.3 ± 4.2
Mean cell haemoglobin (g/dL)	31.2 ± 1.6	31.3 ± 1.8
Mean cell haemoglobin concentration (g/dL)	34.4 ± 1.2	34.6 ± 0.9
Neutrophils ($\times 10^9$/L)[a]	3.5 ± 1.1	3.5 ± 1.2
Lymphocytes ($\times 10^9$/L)[a]	2.3 ± 0.8	2.2 ± 0.8
Monocytes ($\times 10^9$/L)[a]	0.5 ± 0.2	0.5 ± 0.2
Eosinophils ($\times 10^9$/L)[a]	0.2 ± 0.1	0.1 ± 0.1
Basophils ($\times 10^9$/L)[a]	0.0 ± 0.02	0.0 ± 0.03

n = 25, unless otherwise indicated ([a]n = 23).

Table 9. Liver function test results

Parameter	Baseline	Visit 3
Total bilirubin (μmol/L)	9.3 ± 6.2	9.9 ± 6.0
Aspartate aminotransferase (AST) (U/L)	27.4 ± 10.8	24.7 ± 8.1
Total protein (g/L)	75.6 ± 4.1	74.6 ± 3.8
Globulin (g/L)	32.2 ± 3.6	31.6 ± 3.6
Alkaline phosphatase (U/L)	77.7 ± 35.7	77.4 ± 34.2
Alanine aminotransferase (ALT) (U/L)	24.6 ± 13.4	24.4 ± 14.1

All data expressed as mean ± standard deviation (n = 31).

DISCUSSION

There are a wide variety of arthritis and other rheumatic conditions (AORC). They can either be primary in nature or secondary to other disorders and are associated with substantial economic and social costs. AORC demands a considerable amount of health care use and significantly affects the psychological status of the individuals and their families (Yelin and Callahan, 2005). Bodily pain and functional disorders associated with AORC greatly reduce the patient's quality of life (Reginster, 2002). Relieving pain suffered by the patient is the single most important goal that the health care practitioner wishes to achieve (Singer *et al.*, 2000).

In recent years, NSAIDs have been developed which are thought to be more specific in dealing with inflammation and are less likely to irritate the digestive (gastrointestinal) system. However, long term safety data for the newest of these preparations, along with Devil's claw, are still lacking.

There are over 20 published studies looking at the effects of Harpagophytum in the treatment of rheumatic disorders, most of which are open and uncontrolled (Wegener, 1999). This study was carried out to assess the effectiveness, safety and tolerability of Harpagophytum 480 mg tablets in patients with general rheumatic disorders.

The results of this study indicate that Harpagophytum (480 mg b.i.d.) could be an effective and well-tolerated treatment for patients with general rheumatic disorders. It had no effect on blood count results and did not cause any measurable hepatocellular injury in those patients studied.

The most striking results of the study were seen in pain reduction. Indeed, pain levels were significantly reduced in all joints affected by general rheumatic disorders during this study. In addition, more than 60% of patients taking analgesics for joint pain at baseline had either reduced their intake or completely stopped taking them at endpoint thus showing that *Hp* had a positive impact on concomitant medication. Similar findings from other studies have been published. Chantre *et al.* (2000) reported that Harpagophytum significantly reduced the intake of NSAIDs compared with diacerhein. Pain reduction greatly enhances quality of life. As shown in the SF-12, patients were in a better physical and emotional state at the end of the study.

The patient experience of taking Harpagophytum was very favourable, as illustrated by the compliance data and with their medication. On the hypothetical

question if they would agree to continue taking Harpagophytum in the future the majority of the patients answered with yes.

A major problem with general rheumatic disorders is that patients also experience exacerbations (flares). Chrubasik *et al.* (1996) investigated the effects of Harpagophytum in a double-blind, placebo controlled study in patients with acute exacerbations of chronic low back pain. At the end of the study, nine patients in the treatment group and one patient in the placebo group were pain free. A 20% improvement in the low back index was also observed in patients taking Harpagophytum, compared with 8% in patients taking placebo. There is anecdotal evidence that long-term use of Harpagophytum reduces the frequency and severity of these flares. Therefore NSAIDs could be the recommended treatment for patients during flares.

A few patients had mild to moderate adverse events which affected the digestive system. Overall, the tolerability was rated good by 87% of patients. These tolerability findings are comparable to earlier studies. For example, Chantre *et al.* (2000) compared the tolerability of Harpagophytum with that of diacerhein in 122 patients with osteoarthritis of the knee and hip. According to their findings, 26 patients taking diacerhein and 16 taking Harpagophytum reported one or more adverse events. The most frequently reported event was diarrhoea, which occurred in 8.1% and 26.7% of Harpagophytum and diacerhein patients, respectively.

Based on the results of this study, it can be concluded that Harpagophytum 480 mg tablets has the potential to be an effective and well-tolerated therapy. The findings are in line with those for other Harpagophytum preparations described in the literature for the treatment of general rheumatic disorders. The results from this study indicate that Harpagophytum is suitable for medium-term use (2 months) and is associated with few gastrointestinal side effects. Devil's Claw is therefore a potential treatment option for mild to moderate degenerative rheumatic disorders.

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