Phytomedicine ▮ (▮▮▮▮) ▮▮▮–▮▮▮

Contents lists available at ScienceDirect

Phytomedicine

journal homepage: www.elsevier.de/phymed

Rose hip herbal remedy in patients with rheumatoid arthritis – a randomised controlled trial

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ARTICLE INFO

Keywords:
Rheumatoid arthritis
HAQ
Disability score
Quality of life
Rose hip
Rosa canina

ABSTRACT

Objective: To investigate if standardised powder made from rose-hip (*Rosa canina*) can reduce the symptom score in patients with rheumatoid arthritis.
Methods: In a double-blind placebo-controlled trial, patients with rheumatoid arthritis (RA) according to ARA/ACR criteria were randomised to treatment with capsulated rose-hip powder 5 g daily or matching placebo for 6 months at two outpatient clinics in Berlin and Copenhagen. Primary outcome variable was Health Assessment Questionnaire (HAQ) at 6 months, secondary outcome included DAS-28, physician's global evaluation of disease activity, RAQoL, SF-12 and concomitant pain medication.
Results: In a total of 89 patients (90% female, mean age 56.6+11.3 years, mean disease duration 12.8+9.6 years) HAQ-DI in the rose-hip group improved by 0.105 ± 0.346, whereas in the placebo group it worsened by 0.039 ± 0.253 (p adjusted=0.032). In the HAQ Patient Pain Scale no significant differences were observed between both groups. In the HAQ Patient Global Scale a trend was seen favouring rose-hip (p=0.078). The DAS-28 score yielded improvement in the rose-hip group of 0.89 ± 1.32 and in the placebo group of 0.34 ± 1.27 (p=0.056) indicating moderate clinical relevance. The Physicians Global Scale demonstrated more improvement in the rose-hip compared to the placebo group (p=0.012). RAQoL and SF-12 physical score improved significantly in the rose-hip group compared to placebo, whereas SF-12 mental score remained unchanged. Intake of pain medication was not different between the groups. Per-protocol analysis confirmed these results.
Conclusion: The results indicate that patients with RA may benefit from additional treatment with rose hip powder.

Introduction

Rheumatoid arthritis (RA) is a chronic, inflammatory and autoimmune disorder that affects the joints in a polyarticular manner. The most prominent symptoms are pain on palpation, arthralgia, swollen joints, stiffness of joints and loss of function. If the diagnosis is established, treatment is usually started with disease-modifying anti-rheumatic drugs (DMARDs) such as methotrexat or leflunomide. For reducing pain and stiffness in RA patients the therapy is often supplemented with pain medication such as paracetamol or non-steroidal anti-inflammatory drugs, if necessary including COX-2 inhibitors. Many of the different treatments are expensive for the society as well as for the patient. A recent study in Germany for example estimated that the RA related direct cost during one year were 2312 Euro per patient (Ruof et al. 2003). Furthermore all these different types of medication each have potential side effects (Vane and Botting 1998; Rodriquez and Hernandez-Diaz 2000; Mukherjee et al. 2001).

It seems therefore of relevance to develop new strategies for treating pain in muscle and joints including medication that should be affordable and associated with a minimum of side effects. Evening primrose oil containing gamma linolenic acid (GLA) has been claimed to reduce morning stiffness and global assessment of disease severity in patients with rheumatoid arthritis. Evening primrose oil however, has well known side-effects such as gastric complications e.g. loose stool, nausea and beside this also headache (Leventhal et al. 1993; Leventhal et al. 1994; Zurier et al. 1996). Fish oil (n-3 fatty acid) was suggested to reduce pain and stiffness in patients suffering from RA (Fortin et al. 1995). In addition vegetarian diet has also been shown to reduce symptoms in RA (Kjeldsen-Kragh et al. 1991).

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0944-7113/$ - see front matter © 2009 Elsevier GmbH. All rights reserved.
doi:10.1016/j.phymed.2009.09.003

A standardised powder from rose hip (*Rosa canina*) was reported to inhibit chemotaxis of neutrophils and to lower C-reactive protein in healthy volunteers and in patients with osteoarthritis (Kharazmi and Winther 1999). These findings were followed by randomised clinical studies in patients with osteoarthritis indicating that rose hip powder reduced pain moderately and improved physical activity (Warholm et al. 2003; Winther et al. 2005).

The aim of the present randomised trial was to evaluate the efficacy of rose hip powder on symptoms in patients with RA.

Materials and methods

Study design and population

The study design was randomized, double-blind, placebo-controlled and parallel. Patients were randomised centrally (computer-generated) in blocks of four. The study was approved by the local ethics committees and performed according to the guidelines for Good Clinical Practice. Included were patients aged 18 years and over with RA according to the revised American Rheumatism Association criteria for the classification of rheumatoid arthritis (Arnett et al. 1988), who gave written informed consent. Exclusion criteria were as follows: Lupus erythematosus present, patients with known allergy to plant products, patients with kidney or liver disease, drug abusers, patients with psychiatric disease and pregnancy. The participants were recruited from 04/2005 to 08/2006 at one outpatient clinics-in Berlin, Germany and two clinics in Denmark.

Intervention

Participants were instructed to take 5 capsules in the morning and 5 capsules in the evening, each capsule containing 0,5 g of rose hip powder or placebo of a similar taste, appearance and smell. In addition, usual care was continued in both groups. Active treatment comprised biological standardised rose hip powder produced by HybenVital, Langeland, Denmark, trade name LitoZin/i-flex. Details regarding the production of the present standardized rose hip powder are provided elsewhere (Winther et al. 2005).

Outcomes

The primary outcome was the Health Assessment Questionnaire (HAQ) disability index (DI) (Wolfe 2001) at 6 months. The HAQ-DI is derived from a questionnaire comprising eight subscales: dressing, arising, eating, walking, reaching, gripping, hygiene, and carrying out common activities. The highest scores in each category are the summed up with requirement of aids or devices taken into consideration and divided by the number of categories yielding a disability index that ranges from 0-3 with higher scores indicating more disability. The HAQ also includes two visual analogue scales (VAS), a patient pain scale and a patient's global scale both raging from 0-100.

Additional outcomes included the disease activity score (DAS-28) is a combined index of swollen and tender joint counts as well as erythrocyte sedimentation rate (ESR) and the patient's self-evaluation of disease activity (Prevoo et al. 1995). Presented as a number between 0 and 10, DAS-28 indicates how active the RA is at this moment (higher scores indicating higher activity). The physician′s evaluation of disease activity is a VAS scale range 0-100. Health-related Quality of Life (QoL) was measured using the Short form (SF)-12 as a generic and also the RA QoL as a disease specific instrument. The SF-12 has a well-documented psychometric history as an excellent measure of HRQoL. The scales are aggregated to comprise the physical component summary (PCS) and the mental component summary (MCS) measures, higher scores indicating better HRQoL. The RAQoL comprises of 30 questions, lower scores indicate a better outcome (De Jong et al., 1997). A hybrid measure that retains inflammation on the ACR 20, ACR 50 and ACR 70, and combine this data with the mean percentage improvement in core set measures was suggested-but not applied. This weakens the study.

Medication was recorded according to the physician′s CRF and a patients' diary, to be documented during the study period.

Evaluation

At the time of study enrolment sociodemographic data were documented and the participants were asked to fill out 3 questionnaires (HAQ, RAQoL, SF-12 [German/Danish version respectively]). The researcher filled out the case record form (CRF) which also included a detailed description of concomitant medication of any kind. Also, the Disease Activity Score (DAS-28) and the physician′s evaluation of disease was recorded. Routine blood samples for haemoglobin, C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) were taken and analysed. Finally blood for evaluation of cytokines, tumour necrotic factor alpha (TNF alpha) and lipid profile was isolated and placed in a refrigerator for later analysing. The patient was encouraged to continue unchanged with his/her daily medication. Also the participant was instructed to write down his/her daily consumption of study medication, including any concomitant medication.

Further visits were scheduled after 1 and 3 months for handing out new medication and diaries, monitoring compliance, asking about a change in medication and adverse effects. Also, the HAQ was filled out by the participants at both visits. The RAQoL and SF-12 were also filled out at 3 months. At the final visit at months 6 participants were again asked to fill out the 3 questionnaires (HAQ, RAQoL, SF-12 [German/Danish version respectively]) and the physician filled out the DAS28, the VAS scale and sampled blood.

The participants had to contact the study centres in case of any adverse effects. Patient Compliance was ascertained by counting study medication after each treatment period and by monitoring the use of concomitant medication taken.

Statistical analysis

The protocol stated that a minimum of 80 patients should be randomised into the study, in order to get at least 30 patients, in each arm, who complete the study. In similar studies using the present rose hip powder and placebo on patients with osteoarthritis, this number of patients resulted in clinically relevant differences (Warholm et al. 2003; Winther et al. 2005) and the present amount of patients would yield a less than 5% risk of type 1 error and a less than 10% risk of a type 2 error. After finishing this study on patients with rheumatoid arthritis, a sample size estimation yielded 53 subjects in each group to detect with 80% power a difference of 0.22 in HAQ-DI means (considered clinically relevant (Bruce and Fries 2003)) assuming a standard deviation of 0.4 and using a two-sided significance level of 0.05. Data were analysed under blind conditions for 3 populations: (1) Intention to treat (ITT), (2) predefined group of patients who had participated in the trial for at least for 3 month, (3) patients who participated the entire 6 month (per-protocol population). SAS Version 9.1 was used (SAS Institute, Cary, NC). Mann-Whitney and Fisher's Exact

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Test were applied to measure differences in baseline characteristics and outcomes.

The main analysis examined differential impact of treatment in an ITT analysis by comparing change scores (3 months minus baseline and 6 months minus baseline) between the two groups using an analysis of covariance (ANCOVA) adjusted for baseline value. For participants who discontinued treatment prior to 6 months, their final values were determined using their last observed value carried forward (LVCF).

Examination of baseline factors to be predictors or effect modifiers were performed by tests of interaction between factor and intervention group.

Results and discussion

Patient characteristics

A total of 89 participants were enrolled in the study, 90% female, mean age 56.6 ± 11.3 years, mean RA disease duration 12.8 ± 9.6 years. At baseline there were no relevant differences between the groups (Table 1). After 6 months a total of 15 participants had dropped out during the trial but were included in the intent-to-treat analysis (Fig. 1).

Outcome

Table 2 shows the mean absolute values of the outcome variables in the treatment and the placebo group at baseline, 3 months and 6 months on an intention-to–treat analysis. The primary outcome mean change in HAQ-DI of patients in the treatment group improved i.e. numerically declined after 3 and 6 months treatment, respectively, whereas in the placebo group it worsened i.e. numerically increased (p=0.014 and p=0.032) comparing groups. In the HAQ Patient Pain Scale no significant differences were observed between groups. In the HAQ Patient Global Scale a trend was seen favouring treatment after 6 month of treatment (p=0.078).

These results were supported by instruments of the physician: after 6 month treatment the DAS28 score yielded a higher improvement in the active treatment group of 0.89 ± 1.32 than in the placebo group of 0.34 ± 1.27 (p=0.056) indicating moderate clinical relevance. Likewise, the Physicians Global Scale showed strong (about 30%) improvement in the treatment compared to the placebo group (7%) (p=0.012) when evaluated after 6 month treatment. These observations were supported by QoL assessment: SF-12 physical and RAQoL scores improved (p=0.013 and 0.043 respectively) in the actively treated group compared to placebo, whereas SF-12 mental score remained unchanged. Also there was no significant reduction on pain medication.

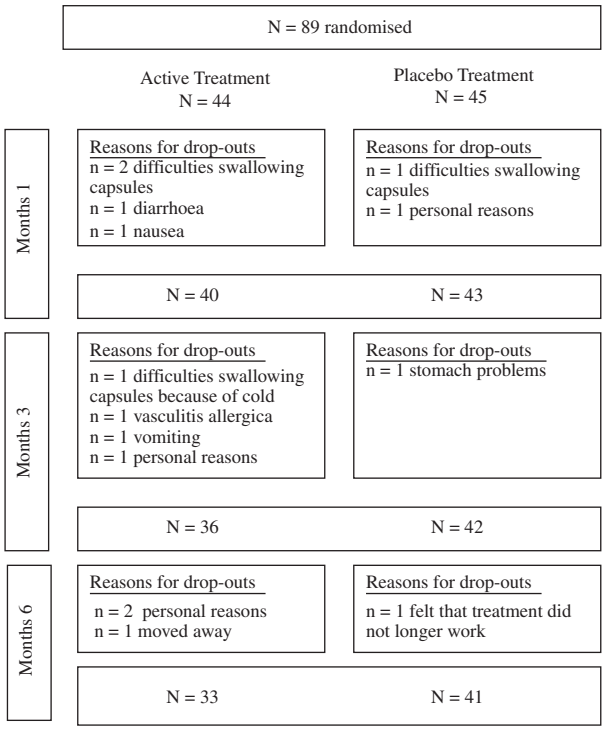

Fig. 1. Flowchart of patients.

Table 1
Baseline characteristics of rheumatoid arthritis participants (N=89).

	Treatment group (N=44)	Placebo (N=45)	p-value
Age (years) (mean ± SD)	57,0 ± 10,6	56,1 ± 12,0	0.915
Female sex (%)	86	93	0.315
Disease duration (years) (mean ± SD)	12,7 ± 9,2	13,0 ± 9,9	0.935
BMI (kg/m2) (mean ± SD)	25,7 ± 4,3	25,2 ± 4,6	0.337
Education (10 years or more) (%)	75	75	1.000
Full-time/part time employment (%)	36	39	0.589
Living alone (%)	30	23	0.628
Smokers (%)	23	11	0.167
Patients using analgesics (%)	46	49	0.830
Patients using NSAID's (%)	64	53	0.390
Patients using Steroids (%)	27	40	0.260
Patients using DMARD's (%)	68	73	0.650
Patients daily consumption of:			
Analgesics (paracetamol units/day)	881 ± 1581	961 ± 3268	0,924
NSAID's (mg/day)	93,4 ± 217	88,9 ± 205	0,263
Steroids (mg/day)	1,4 ± 3,1	1,7 ± 3,0	0,246
DMARD's			
Methotrexat (mg/day)	3,8 ± 16,6	3,7 ± 15,1	0,695
Leflunomide (mg/day)	1,0 ± 4,4	2,0 ± 5,7	0,303
Biological anti-rheumatic drugs (mg/day)	5,0 ± 22,1	2,8 ± 15,3	0,496
Chloroquin (mg/day)	10,0 ± 44,1	18,9 ± 59,9	0,446

The group "Analgesics" contain paracetamol, tramadol and codeine.

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Table 2
Clinical indices of disease activity at baseline, 3 and 6 months in rheumatoid arthritis patients.

	baseline	3 months	6 months	p-value *	p-value * *
HAQ-DI (0-3)					
Active	1.13 ± 0.55	1.00 ± 0.59	1.03 ± 0.58	0.014	0.032
Placebo	1.11 ± 0.76	1.13 ± 0.71	1.15 ± 0.74		
HAQ Pain Scale (VAS)					
Active	44.73 ± 22.75	41.50 ± 23.36	39.82 ± 23.44	0.226	0.209
Placebo	45.56 ± 21.98	47.09 ± 22.14	45.71 ± 23.47		
HAQ Patient's Global Scale (VAS)					
Active	47.55 ± 25.96	41.55 ± 22.62	39.57 ± 25.01	0.225	0.078
Placebo	47.13 ± 21.28	46.44 ± 25.19	47.18 ± 24.13		
DAS28					
Active	4.82 ± 1.33	4.18 ± 1.22	3.93 ± 1.56	0.196	0.056
Placebo	4.71 ± ± 1.01	4.47 ± 1.46	4.42 ± 1.17		
Physician's Global Scale (VAS)					
Active	47.50 ± 19.28	40.43 ± 22.25	33.57 ± 23.72	0.328	0.012
Placebo	48.16 ± 18.31	44.89 ± 23.44	44.64 ± 22.79		
RAQoL					
Active	11.57 ± 6.36	10.20 ± 6.39	10.18 ± 7.22	0.113	0.043
Placebo	10.87 ± 6.68	19.73 ± 6.75	11.09 ± 6.89		
SF-12 physical					
Active	32.91 ± 8.77	35.37 ± 9.51	36.22 ± 9.28	0.515	0.013
Placebo	33.19 ± 9.43	35.95 ± 10.13	33.78 ± 8.86		
SF-12 mental					
Active	49.30 ± 10.44	49.63 ± 10.94	48.46 ± 10.85	0.315	0.954
Placebo	49.13 ± 9.34	48.12 ± 9.75	48.64 ± 9.46		

Data are presented as means ± SD. Intention-to-treat analysis (N=89).
VAS = Visual Analogue Scale 0–100.

* p-value: from ANCOVA- Difference 3 months to baseline adjusted for baseline values.
* * p-value: from ANCOVA- Difference 6 months to baseline adjusted for baseline values.

Table 3
Clinical indices of disease activity at baseline, 3 and 6 months in rheumatoid arthritis patients.

	baseline	3 months	6 months	p-value *	p-value * *
HAQ-DI (0-3)					
Active	1.12 ± 0.53	0.97 ± 0.59	1.00 ± 0.58	0.008	0.023
Placebo	1.09 ± 0.75	1.12 ± 0.70	1.14 ± 0.73		
HAQ Pain Scale (VAS)					
Active	45.31 ± 22.40	40.81 ± 23.42	38.75 ± 23.44	0.228	0.189
Placebo	44.64 ± 21.65	46.29 ± 21.89	44.81 ± 23.27		
HAQ Patient's Global Scale (VAS)					
Active	48.53 ± 25.89	41.14 ± 21.81	38.72 ± 24.75	0.250	0.083
Placebo	46.10 ± 21.03	45.36 ± 25.22	46.14 ± 24.11		
DAS28					
Active	4.87 ± 1.30	4.11 ± 1.16	3.81 ± 1.56	0.146	0.029
Placebo	4.71 ± 1.03	4.45 ± 1.50	4.40 ± 1.19		
Physician's Global Scale (VAS)					
Active	45.58 ± 19.63	36.94 ± 22.10	28.56 ± 22.33	0.209	0.003
Placebo	47.07 ± 18.24	43.60 ± 23.54	43.33 ± 22.83		
RAQoL					
Active	11.92 ± 6.58	10.25 ± 6.66	10.22 ± 7.64	0.093	0.035
Placebo	10.86 ± 6.68	10.71 ± 6.75	11.10 ± 6.90		
SF-12 physical					
Active	33.19 ± 8.24	36.19 ± 9.02	37.23 ± 8.61	0.428	0.008
Placebo	33.74 ± 8.86	36.65 ± 9.52	34.30 ± 8.24		
SF-12 mental					
Active	48.53 ± 10.37	48.96 ± 11.02	47.53 ± 10.80	0.348	0.858
Placebo	48.66 ± 9.45	47.62 ± 9.82	48.20 ± 9.54		

Data are presented as means ± SD. Predefined analysis on patients who participated for 3 month or more, last value carried forward (N=78).

* p-value: from ANCOVA-difference 3 months to baseline adjusted for baseline value.
* * p-value: from ANCOVA-difference 6 months to baseline adjusted for baseline value.

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A pre-defined analysis of all 78 patients who participated for at least 3 month in the trial (Table 3) and analysis of the 74 patients who completed the trial (data not shown) confirmed these results essentially. In addition the DAS-28 score difference became statistically significant.

Several factors were examined as possible predictors or effect modifiers for the treatment effect: sex, age, BMI, centre and employment status. None of these factors showed a significant result (data not shown).

As shown in Table 1, there were no statistically significant difference in the pattern of the consumption of analgesics (paracetamol, tramadol and codeine), NSAID's, steroids and DMARD's at baseline. In addition when the consumption of medicine during the 6 month treatment period was calculated, there was no statistically significant change in the consumption of analgesics, NSAID's, steroids and metrotrexate or other DMARD's in either of the two groups or when comparing groups.

Blood sampling

Additionally blood samples at baseline and 6 months were analysed. There was no statistically significant change in haemoglobin, interleukins, tumour necrotic factor alpha (TNF alpha) and cholesterol level (data not shown). ESR declined in the actively treated group as compared to the placebo group, P-values for the ITT population and for patients participating in the study for three months or more were 0.060 and 0.045, respectively. A similar trend, although not significant, was observed for CRP (data not shown).

Adverse effects

There were 14 reports on side effects in the actively treated group and 26 reports in the placebo group (Table 4). There was one serious event (vasculitis allergica) in the treatment group where the code was broken. However, it was not clear whether this event was related to the study medication as the patient was also taking a number of other medications. Four patients in the treatment group dropped out due to adverse effects, compared with 1 patient in the placebo group (Fig. 1). So far this study did not detect adverse events of any kind, which can be related to the present rose hip and seed powder. This seems to be in correspondence with previous studies of the same powder on patients with osteoarthritis (Warholm et al. 2003; Winther et al. 2005; Christensen et al. 2008).

Table 4
Adverse effects in rheumatoid arthritis patients.

	Active (n)	Placebo (n)
Gastro-intestinal disturbances	5	8
Common cold /Influenza	2	7
Skin Rash /Eczema	2	4
Vasculitis	1	
Elevated diuresis		1
Back problems		1
Swallowing problems	1	
Dizziness		1
Urinary tract infection (UTI)	1	
Headache	1	
Cyst in left breast		1
Pain in hand		1
Weight gain	1	
Sleeping disturbances		1
Elevated blood pressure		1
Total	14	26

Discussion

The present study suggests some benefit of patients with RA treated with the present rose hip powder as indicated in the HAQ-DI and the HAQ Patient Global Scale. The secondary outcomes DAS-28, Physician's Global Scale and QoL assessments RAQoL scores and SF-12 physical support these findings, and no change in the consumption of analgesics, NSAID's, steroids and DMARD's were observed in any of the two groups during the six month treatment period.

The clinical relevant change in HAQ-DI score is given as 0.22 (Bruce and Fries 2003). The average change in the study was a decline of 0.10 in the score of actively treated patients and an increase in the score of 0.04 in the placebo treated group-a modest, although significant change. For that reason a sub analysis was applied on the sub fraction of patients (n=21) who showed a change in HAQ-DI score of 0,22 or more, as the result of 6 month treatment. Fischer's Exact test yielded a table probability (p) of 0.040 in favour of active treatment in the ITT population and of 0.031 in patients who participated in the study for at least 3 month.

There are only few herbal products which were suggested to be effective in RA. A recent Cochrane review concluded that the strongest evidence was found for gamma-linolenic acid (GLA) found in evening primrose oil, borage seed oil and black current seed oil (Little and Parson 2000). All of the GLA studies found some improvement in clinical outcomes but study quality was variable, making it difficult to draw conclusive results. However, the better quality studies suggested potential relief of pain, morning stiffness and joint tenderness. In one study where gamma-linolenic acid was given for 6 month, a time period comparable to the present study, the number of tender joints declined by 36% in patients completing the study (Leventhal et al. 1993). The number of tender joints, which is a part of the DAS-28 score used as direct outcome in the present study, declined by 45% in per protocol patients ($p < 0.042$). It is interesting to note that both products contain plant fatty acids and the structure of the galacto-lipid, GOPO, isolated from the present rose hip powder has some similarities with gamma-linolenic acid (Larsen et al. 2003).

Fish oil is another product of natural origin which has shown significant improvement in RA. A recent meta-analysis demonstrated that dietary fish oil supplementation significantly reduced tender joint count after long term treatment as compared with placebo (Fortin et al. 1995; Cleland et al. 1988). Like the present rose hip powder, fish oil contains long chain fatty acids which act anti-inflammatory. It is encouraging to observe that diet both from fish and from selected plant species can modify the number of tender joints and symptom score in RA.

An inhibition of neutrophil chemotaxis was earlier shown using the present rose hip powder and it was further demonstrated that the inhibitory effect was related to GOPO (Kharazmi and Winther 1999, Larsen et al. 2003). A recent paper indicates that this standardized rose hip powder contains lipophilic COX inhibiting compounds (Jäger et al. 2007). These findings are further supported by in vivo animal studies showing an anti-inflammatory and anti-nociceptive activity of fruits from rose hip (Orhan et al. 2007) and by studies on human articular cells showing that the present rose hip powder and the galactolipid GOPO in particular show anti-inflammatory and chondro-protective properties (Schwager et al. 2008). It was likewise demonstrated that rose hip, which is rich in bioactive polyphenoles, reduces inflammatory injuries leading to tissue damage in mouse colon (Håkansson et al. 2006). The present study demonstrated a reduction in ESR, suggesting an anti-inflammatory action.

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The rose hip powder did not produce side effects different from what was observed for placebo, when added to the already initiated standard RA treatment. This safety profile is consistent with earlier studies on patients with osteoarthritis (Warholm et al. 2003; Winther et al. 2005, Christensen et al. 2008).

Rose hip was shown to have strong anti-oxidant capacity compared with other dietary plants (Halvorsen et al. 2002). Calculated from Halvorsens estimates on different fruits, vegetables and berries it was estimated that there is more than a 1000-fold difference in total antioxidant capacity among various dietary plants with rose hip being the most powerful anti-oxidant of all investigated plants. Extracts from rose hip were also shown to reduce the release of reactive oxygen species from polymorphonuclear neutrophils suggesting a protective effect on different tissues (Kharazmi and Winther 1999; Daels-Rakotoarison et al. 2002).

Although the pathophysiological background of RA is not fully elucidated, reactive oxygen species appears part of its pathogenesis (Biemond et al. 1984). Cartilage loss occurs as a consequence of enzymatic degradation by metalloproteinases, the synthesis of which is enhanced by cytotoxic free radicals such as nitric oxide (NO) present in the inflamed areas (Martel-Pelletier et al. 1994, Murrell et al. 1995). Total plasma antioxidant capacity was also reported to be reduced in RA (Sarban et al. 2005) and it is suggested that anti-oxidants to some extend can prevent symptoms of RA by modifying cartilage destruction (Schwager et al. 2008). This hypothesis may also explain why a sustained vegan diet was observed to reduce the symptom score and number of tender joints in patients with RA (Kjeldsen-Kragh et al. 1991) and why a vegan diet rich in antioxidants were reported to reduce disease activity in patients with RA (Hänninen et al. 2000).

The only parameter with significant effects already after 3 months of treatment was the HAQ-DI. Since after 6 months several further outcome measures, such as DAS-28, physician's global evaluation, HAQoL and SF-12 physical showed improvement, a delayed onset of effects of the present remedy is suggested. This is in agreement with observations using other plant and fish fatty acids which also show a slow but sustained onset in RA patients (Leventhal et al. 1993; Fortin et al. 1995). The biochemical background for the slow onset still needs to be clarified. A slow onset and carry over effects were detected in a study where the present rose hip powder was given to patients with osteoarthritis (Winther et al. 2005).

From a public health perspective the present results are interesting since they may guide in developing new therapeutic approaches for RA with enhanced clinical effectiveness. Particularly in the case of potentially disabling disorders with high medical and economic burden such as RA such new strategies are warranted.

In conclusion: The present trial was small and was not to well powered. And thus, though promising, the values should be taken with precaution. Therefore, studies with higher sample size and adequate power for multivariate analysis are warranted. Future research should also include dose-finding studies and testing of different rose hip extractions.

Acknowledgement

We appreciate the support of the nursing staff including Mette Strandberg, Helle Högstad and Susanne Eriksen and the laboratory assistants Ellen Udh and Marjan Yousifi. The study was supported by grants from Dansk Droge and Hyben Vital ApS, Denmark.

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Please cite this article as: Willich, S.N., et al., Rose hip herbal remedy in patients with rheumatoid arthritis – a randomised controlled trial. Phytomedicine (2009), doi:10.1016/j.phymed.2009.09.003

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Please cite this article as: Willich, S.N., et al., Rose hip herbal remedy in patients with rheumatoid arthritis – a randomised controlled trial. Phytomedicine (2009), doi:10.1016/j.phymed.2009.09.003