Special extract of BOSWELLIA serrata (H 15)*
in the treatment of rheumatoid arthritis

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Summary

H 15, a special extract of the gum resin of Boswellia serrata (BS) is effective in the treatment of rheumatoid arthritis (RA). These findings were obtained in more than 260 patients by using a range of different clinical approaches for evaluation. The criteria for assessment were mainly joint swelling, pain, erythrocyte sedimentation rate (ESR), stiffness, additional use of NSAID, side effects and tolerance. The therapeutic action was mainly proven by comparing H 15 with a placebo standard therapy. H 15 is:
- normally not used for acute pain therapy;
- a disease-modifying agent and can replace other disease-modifying therapies;
- beneficial in early use;
- also beneficial when used with current disease-modifying drugs;
- well tolerated and safe in early use and long-term therapy.

Key words: Rheumatoid arthritis, Boswellia serrata, H 15, efficacy, clinical studies.

Introduction

The gum resin of Boswellia serrata, also known as incense or Olibanum, has been used worldwide for centuries as a traditional treatment for many health problems (Martinetz, Lobs et al., 1988).

Early interest in Ayurveda at the end of the 1970s brought a group of medical practitioners (organized into the Research and Development-Company Ayurmedica) into contact with Ayurvedic medicines.

H 15 was of special interest as an extract because of its therapeutic claims regarding rheumatic disease – an area where neither allopathic medicine nor phytotherapy offer satisfying treatment.

Patients treated with H 15 had reported decreased symptoms and improved wellbeing. Due to these promising results, a systematic investigation of the drug was started in 1985. Requirements regarding toxicity, safety and pharmaceutical quality were observed. However as physicians our main focus was on the therapeutic effects in order to determine H 15's efficacy.

Rheumatoid arthritis (RA) was deemed the most important target due to the unsatisfactory therapeutical situation faced by physicians and patients. This situation can be summarized as follows:
- the disease is not fully understood;
- only a few disease-modifying drugs besides NSAID are available, and most of them are primarily used for other diseases;
- their potential to modify the disease at all is almost never understood;
- side-effects are obvious and well known.

Many difficulties had to be overcome at the beginning of the studies. The attitude towards phytotherapy in the medical community was not very open in the early 1980s compared to today, especially concerning rheumatic diseases. At that time the recently discovered method of action of Boswellia serrata and H 15 (Safayhi et al., 1992) was not yet clear. The therapeutical standard was mostly preferred by the medical doctors when H 15 was offered for a clinical study. As a result, only mal- or non-responders to the standard therapy could be included in clinical...
studies – not the best conditions for starting a clinical trial.

The methods of scientifically evaluating therapeutic long-term effects are still under discussion in the field of rheumatoid arthritis (Pincus, 1993). Clear predictors do not exist, the main criteria for biometrical evaluation are numerous, and exacerbations and remissions are not predictable. Long-term studies for any comparison did not exist.

For this reason, both explanatory and confirmatory approaches were chosen to evaluate H15’s effectiveness. Both were needed not only to confirm the clinical effects on a statistical basis, but also to discern from the special case studies the characteristics of the drug-information which is at least as important to the physician as statistical evaluation.

Material and Methods

Fingerprint analysis of Boswellia special extract

The fingerprint analysis was performed by TLC and HPLC of the CHCl3-extract of H15. One tablet was grounded in a mortar, soxhlet-extracted with 50 ml CHCl3 p.a. for 1 h and the extract evaporated to dryness. The extract was dissolved in 10 ml ethanol p.a.

TLC: 10 μl of the ethanolic solution were applied to silica gel 60 F254 silicagel plates of Merck. Solvent system: hexene-ethylacetate/glacial acetic acid 70:30:1. Detection: vanillin/H2SO4-reagent (Reagent 1), 1% ethanolic vanillin-sol. (Reagent 2). The TLC plates are sprayed with Reag. 1 followed by Reag. 2. The plates are heated at 110°C for 5–10 min. The following compounds could be detected in Vis: β-amyrin (Rf ~ 0.70), acetylboswellic acid (Rf ~ 0.55) boswellic acid (Rf ~ 0.40) and many other violet spots in the higher and low Rf-range.

HPLC: (see Fig. 1) Column: LiChrocart 125-4 with LiChrosorb RP18 (7 μm) (Merck) and Waters Guard-Pak precolumn modul with C18-material.

Solv. system: from 50% acetonitril (in H2O) linear in 30 min. to 100% acetonitril with 4% 0.1 M phosphoric acid addition.
Flow rate: 1.0 ml/min.; Injection: 10 μl CHCl3-solution;
Detector: HP 1040 A photodiode array (Hewlett Packard); Detection: 200 nm.

All studies have been designed in advance. The dosage administered to the patients was normally 3x2 or 3x3 tablets of H15 as a 400 mg extract of BS.

Study design (see also Table 1):
explanatory: standardized selected case studies which once again are deemed a valid approach to studying the effects of a drug (Pincus 1993)
sel-controlled studies
confirmatory: comparison of H15 to a placebo (even in major nonresponders to standard therapy)
comparison of H15 to a standard therapy (gold)
additional: withdrawing then restarting the therapy, which falls in between both approaches.

The criteria for statistically assessing the disease and H15’s effects were the measurement of joint swelling and joint pain (as per Ritchie index). Further criteria included: ESR, morning stiffness, additional use of NSAID, general health and well-being, side effects and tolerance. Anti nuclear antibodies (ANA) have been tested as well.

Results

Due to the variability of the disease and the corresponding need to adjust the statistics accordingly only a survey without statistical details can be given.

Not all studies yielded the same results under all criteria, but we found definite effects within the following parameters:
Special Extract of *Boswellia serrata* (H 15) in the treatment of rheumatoid arthritis

Table 1.

<table>
<thead>
<tr>
<th>Investigator</th>
<th>Type of trial</th>
<th>No. of patients</th>
<th>Dosage 400 mg (oral)</th>
<th>Duration</th>
<th>Diagnosis</th>
<th>Reference substance</th>
<th>Criteria</th>
<th>Side effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Suschke, Munich 1985</td>
<td>controlled</td>
<td>15</td>
<td>3×1–3×3</td>
<td>1 month</td>
<td>juvenile</td>
<td>chronic arthritis</td>
<td>pain</td>
<td>0</td>
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<tr>
<td></td>
<td>intra-</td>
<td></td>
<td></td>
<td></td>
<td>swelling</td>
<td></td>
<td>swelling</td>
<td></td>
</tr>
<tr>
<td></td>
<td>individual</td>
<td></td>
<td></td>
<td></td>
<td>sensitivity</td>
<td></td>
<td>tolerance</td>
<td></td>
</tr>
<tr>
<td>Schattenkirchner, Munich 1986</td>
<td>do</td>
<td>14</td>
<td>3×3</td>
<td>3 months</td>
<td>a. CP</td>
<td></td>
<td>do</td>
<td>0</td>
</tr>
<tr>
<td>Stroehmann, Bonn 1986</td>
<td>do</td>
<td>20</td>
<td>3×3</td>
<td>3 months</td>
<td>a. CP</td>
<td></td>
<td>do</td>
<td>1 x diarrhoea</td>
</tr>
<tr>
<td>Josenhans, Bad Brahmstedt 1986</td>
<td>do</td>
<td>6 (pilot)</td>
<td>3×3</td>
<td>6 weeks</td>
<td>a. CP</td>
<td></td>
<td>do</td>
<td>0</td>
</tr>
<tr>
<td>Chandrasekaran, Madras 1986</td>
<td>do</td>
<td>30</td>
<td>3×1</td>
<td>6 months</td>
<td>RA</td>
<td></td>
<td>do</td>
<td>0</td>
</tr>
<tr>
<td>Rajagopal, Madras 1987</td>
<td>do</td>
<td>20</td>
<td>3×1</td>
<td>6 months</td>
<td>juv. RA</td>
<td></td>
<td>synovial</td>
<td>0</td>
</tr>
<tr>
<td>Schattenkirchner, Munich 1986</td>
<td>do</td>
<td>14</td>
<td>3×3</td>
<td>3 months</td>
<td>a. CP</td>
<td></td>
<td>do</td>
<td>0</td>
</tr>
<tr>
<td>Kriegel et al., Emmerich/Ratingen</td>
<td>placebo</td>
<td>48</td>
<td>3×3</td>
<td>3 months</td>
<td>a. CP</td>
<td>placebo</td>
<td>do</td>
<td>1 x local</td>
</tr>
<tr>
<td>1987</td>
<td>controlled</td>
<td></td>
<td></td>
<td></td>
<td>placebo</td>
<td></td>
<td>urticaria</td>
<td></td>
</tr>
<tr>
<td>Heimstädt et al., Bad Aibling</td>
<td>do</td>
<td>33</td>
<td>3×3–3×2</td>
<td>3 months</td>
<td>a. CP</td>
<td>do</td>
<td>do</td>
<td>0</td>
</tr>
<tr>
<td>1988</td>
<td>reference</td>
<td></td>
<td></td>
<td></td>
<td>oral Gold</td>
<td>do</td>
<td>do</td>
<td>1 x nausea</td>
</tr>
<tr>
<td>Hunstein et al., Heidelberg 1990</td>
<td>reference</td>
<td>60</td>
<td>3×2</td>
<td>6 months</td>
<td>a. CP</td>
<td>oral Gold</td>
<td>do</td>
<td>0</td>
</tr>
<tr>
<td>Lohokare, Poona 1985</td>
<td>reference</td>
<td>104</td>
<td>3×1½</td>
<td>1 month</td>
<td>OA</td>
<td>Paracetamol</td>
<td>do</td>
<td>2 x local</td>
</tr>
<tr>
<td>Tripathi, Benares 1985</td>
<td>4×6 (7) groups</td>
<td>25</td>
<td>3×1</td>
<td>2 months</td>
<td>RA</td>
<td>a) Boswellia P.</td>
<td>walking time</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>b) Nux vomica P.</td>
<td>sensitivity</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>c) a+b together</td>
<td>total score</td>
<td></td>
</tr>
</tbody>
</table>

CP = RA = chronic polyarthritis  
juv. RA = juvenile chronic arthritis  
a = active  
OA = osteoarthritis of the knee joints

- H15 produced a significant reduction in swelling and pain compared to the placebo (p < 0.05);  
- ESR was significantly reduced in one study (p < 0.05).  
- Morning stiffness was often reduced;  
- The patients often could considerably reduce their intake of NSAID during the course of treatment;  
- The patients’ general health and well-being improved.

One criteria which had not been foreseen but which turned out to be very important was the incidence of need for emergency treatment by patients suffering a sudden aggravation of symptoms. In all controlled studies with H15 there were significantly fewer emergency interventions required than with control. This cannot be seen as a confirmatory proof, since it was not taken as a main criterion, but can be used as an impetus for further studies.

Summarizing the results of the criteria in different studies the picture for H15 is as follows:

1. The therapeutic potential was seen by comparing H15 with the placebo in patients suffering from RA for several years and non- or mal-responding to the standard therapy, a kind of negative selected group (Letzel et al., 1994).
2. Compared to standard therapy, H15 was slightly more efficacious than gold but not significantly.
3. The positive therapeutic influence of H15 was evident in several cases studies after the medication was withdrawn then restarted.
4. Selected patients malresponding on different standard therapies experienced a clear advantage with H15. This was especially evident in children suffering from juvenile chronic arthritis.
5. The tolerance was very good. Side-effects to H15 have been very mild.

All clinicians and physicians who had participated in the studies are highly specialised in rheumatology. Most of the studies have been done at clinics specializing in rheumatology or at outpatient clinics for rheumatology at University hospitals. As a result, the findings of the placebo-controlled studies have been accepted by and presented to the Annual Conference of the German Association for Rheumatology at Berlin (Letzel et al., 1994).

Conclusions

On the basis of the scientific data and the clinical findings we can summarize the following: H15 is effective in the treatment of rheumatoid arthritis and the following clinical characteristics have been found to be of importance for those administering it:

- H15 is normally not used for acute pain therapy;
- H15 is a disease-modifying agent and can replace other disease-modifying therapies;
- Early use of H15 is beneficial;
- H15 can be beneficial as an adjunct to current disease-modifying drugs;
- H15 is well tolerated and shows high levels of safety for early use and long-term therapy;
- The long-term effects of H15 on the joints and the anatomic and functional structures are not yet clear (as is also true for so-called standard therapy). The initial evidence shows that H15 does have positive effects in this area as well;
- Although H15's efficacy has only been demonstrated scientifically for Rheumatoid arthritis (RA) so far, its range of application also extends at least to chronic rheumatic complaints with inflammatory activity.

**Discussion**

Several questions remain open and further studies are required, especially to answer the following points:
1. Why do only 50-60% of the patients respond to the therapy with H15?
2. What are the long-term effects (more than two years)?
3. What is H15's influence on the deterioration and destruction of the anatomic structure of the joints?

When evaluating H15 one should not forget the present unsatisfactory therapeutic situation in rheumatology today. These unanswered questions for H15 hold for the standard therapy as well.

The number of patients treated with H15 and the treatment time span should be increased to obtain more information on RA. Further studies are planned for the future.

Meanwhile thousands of patients in Germany are benefitting from H15 besides the patients who experienced improvement during the clinical investigation and those residents of other countries who already use H15 as a traditional drug.

Until 1992, H15 was considered by the health authorities as a known medicine from a traditional origin. One main reason why H15 is not yet approved is that the same health authorities are just now reevaluating H15 as an unknown or new chemical entity (NCE) requiring special data for approval. This situation makes little sense when one compares the risk-benefit ratio of standard medication against that of H15 and considers the information collected over thousands of years worldwide for the gum resin of *Boswellia serrata* (Martinetz et al., 1988).

**References**


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