FORMULATIONS FOR THE TREATMENT OF ARTHRITIS CONDITIONS

FIELD OF THE INVENTION

The present invention relates to formulations comprising combinations of analgesic/anti-inflammatory, immunomodulating and cartilage-reconstructing agents for the treatment of rheumatoid arthritis and, more generally, of arthritis conditions.

The combination of these agents, acting through different mechanisms of actions, reduces pain and prevents the progression of articulation injuries.

TECHNOLOGICAL BACKGROUND

Rheumatoid arthritis is a chronic degenerative disease which affects a large portion of the elderly, causing serious problems to patients. The pathogenesis of rheumatoid arthritis and arthritis conditions is due at first to the immune system, and subsequently to inflammatory conditions which erode the intra-articular surfaces causing deforming damages which are irreversible and painful.

DISCLOSURE OF THE INVENTION

The present invention relates to compositions comprising a combination of active principles capable of inducing particularly effective therapeutic effects, without important side effects even after prolonged treatments.

The pharmaceutical formulations of the invention comprise:

- pure saligenin or derivatives thereof or extracts containing them selected from saligenin-enriched *Salix rubra* extract;
- substantially pure boswellic acid or a semi-synthetic derivative thereof or a boswellic acid-enriched *Boswellia serrata* extract;
- procyanindins from *Vitis vinifera* or from *Camellia sinensis* or rhein or lipophilic derivatives thereof;

- N-acetyl-glucosamine;
- glucuronic acid or glucuronolactone.

Examples of saligenin derivatives comprise the acetic or butyric esters, whereas examples of boswellic acid derivatives comprise pharmaceutically acceptable salts or esters.

The formulations of the invention preferably comprise:

- *Salix rubra* extract containing 25% by weight of saligenin;
- *Boswellia serrata* extract containing 20% by weight of boswellic acid;
- procyanindins from *Vitis vinifera* or from *Camellia sinensis* optionally complexed with phospholipids or rhein or lipophilic derivatives thereof;
- N-acetyl-glucosamine;
- glucuronic acid or glucuronolactone.

The *Salix rubra* extract, the *Boswellia serrata* extract, procyanindins, N-acetyl-glucosamine, glucuronic acid or glucuronolactone are preferably present in the formulations in 2:1:1:1:1 weight ratios, respectively.

The formulations will contain typically 100 to 500 mg of 25% *Salix* extract, 50 to 150 mg of procyanindins optionally in the form of complexes with phospholipids, 20 to 200 mg of *Boswellia serrata* extract, 10 to 500 mg each of glucosamine and glucuronic acid or glucuronolactone.

The proanthocyanidins from *Vitis vinifera* can be obtained according to what disclosed in GB-A-1541469 or FR-A-2092743 or in EP 348781, while the corresponding phospholipid complexes are known from US 4.963.527; *Camellia sinensis* extracts are disclosed, for example, in EP 814823.

Boswellia and boswellic acid extracts can be prepared according to known methods, and are commercially available as well the saligenin-enriched *Salix rubra* extracts.

The formulations will be in the form of soft- or hard- gelatin capsules, tablets or other forms suitable for the oral administration. Preferred are the

capsules containing *Enothera biennis* oil as the carrier.

The procyanindins from *Vitis vinifera* or *Camellia sinensis* exert anti-radicalic action and inhibit proteoglycans-hydrolysing metal-proteases; they also synergistically interact with the cyclooxygenase 2 (COX-2) inhibiting components present in the *Salix* and *Boswellia* extracts.

As an alternative to proanthocyanidins, certain anthraquinones, mainly rhein or lipophilic derivatives thereof such as diacerhein, may be used, which reduce cell proliferation and stimulate proteoglycan synthesis.

N-Acetyl-glucosamine, glucuronic acid or glucuronolactone, which can be considered the building blocks of the connective tissue, complete the therapeutic profile of the formulations of the invention, as they promote the resynthesis of proteoglycans in the joints, which is an important restoration process that, together with the aforementioned factors, can contribute to a symptomatic improvement.

The compositions of the invention can be administered for prolonged times, in one or repeated daily administrations, until recovery or relief from the symptoms.

The following examples further illustrate the invention.

Example I - Preparation of cellulose capsules

Each capsule contains:

Salix rubra extract (25% in saligenin)		200 mg
Boswellia serrata extract (20% in boswellic acid)		100 mg
Green Tea extract (70% in procyanidins)		100 mg
N-Acetyl-glucosamine		100 mg
Glucuronolactone		100 mg
Enothera biennis oil	q.s. to	700 mg

Example II - Preparation of capsules

Each capsule contains:

Salix extract (25% in saligenin)		200 mg
Boswellia serrata extract (20% in boswellic acid)		100 mg
Diacerhein		100 mg
N-acetyl-Glucosamine		100 mg
Glucuronolactone		100 mg
Enothera biennis oil	q.s. to	700 mg

The formulation of the Example I, when administered to patients suffering from rheumatoid arthritis or arthritis conditions, showed consistent clinical results in terms of pain reduction, better mobility of the affected limbs, biopsic examinations of the joints and sense of well-being.

CLAIMS

1. Formulations comprising:

- pure Saligenin or derivatives thereof or extracts containing them selected from saligenin-enriched *Salix rubra* extract;
- substantially pure boswellic acid or a semi-synthetic derivative thereof or a boswellic acid-enriched *Boswellia serrata* extract;
- procyanindins from *Vitis vinifera* or from *Camellia sinensis* or rhein or lipophilic derivatives thereof;
- N-acetyl-glucosamine;
- glucuronic acid or glucuronolactone.

2. Formulations as claimed in claim 1 comprising:

- *Salix rubra* extract containing 25% by weight of saligenin;
- *Boswellia serrata* extract containing 20% of boswellic acid;
- procyanindins from *Vitis vinifera* or from *Camellia sinensis* optionally complexed with phospholipids or rhein or lipophilic derivatives thereof;
- N-acetyl-glucosamine;
- glucuronic acid or glucuronolactone.

3. Formulations as claimed in claim 1 wherein the *Salix rubra* extract, the *Boswellia serrata* extract, procyanindins, N-acetyl-glucosamine, glucuronic acid or glucuronolactone are present in 2:1:1:1:1 weight ratios, respectively.

4. Formulations as claimed in claim 2 containing 100 to 500 mg of 25% *Salix rubra* extract, 50 to 150 mg of procyanindins optionally in the form of complexes with phospholipids, 20 to 200 mg of *Boswellia serrata* extract and 10 to 500 mg each of glucosamine, glucuronic acid or glucuronolactone.

5. Formulations as claimed in any one of claims 1-3 in the form of capsules containing *Enothera biennis* oil as the carrier.

6. The use of a combination of:

- pure Saligenin or derivatives thereof or extracts containing them selected from saligenin-enriched *Salix rubra* extract;
- substantially pure boswellic acid or a semi-synthetic derivative thereof or a boswellic acid-enriched *Boswellia serrata* extract;
- procyanindins from *Vitis vinifera* or from *Camellia sinensis* or rhein or lipophilic derivatives thereof;
- N-acetyl-glucosamine;
- glucuronic acid or glucuronolactone;

for the preparation of pharmaceutical, nutraceutical or dietetic compositions for the treatment of rheumatoid arthritis and arthritis conditions.