

## Anti-inflammatory and chondroprotective activity of prodelphinidins isolated from *Ribes nigrum* leaves.

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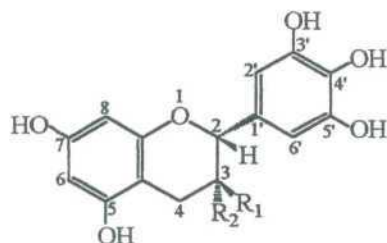
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Black-currant leaves are traditionally used in Europe for the treatment of rheumatic disease. The anti-inflammatory activity (in carrageenan-induced rat paw-oedema) is mainly due to prodelphinidins [1]

Moreover, these prodelphinidins have a profile of a chondroprotective medicament.

Two dimers (1), (2) and a trimer (3) have been tested. They act on the model studied by:

- significantly increasing the production of proteoglycans, assayed by the radio immunological method, in the culture medium and in the newly-formed cluster;
- significantly increasing the production of type II collagen assayed by the radio immunological method, in the culture medium and in the newly-formed cluster;
- significantly reducing the production of prostaglandins E2 in the culture media during the first two culture periods from the 1st to the 4th day, and from the 4th to the 8th day;
- significantly reducing the OH° free radicals produced in the presence of either KMB, or linoleic acid.



GC = gallocatechin R<sub>1</sub>=OH R<sub>2</sub>=H

EGC = epigallocatechin R<sub>1</sub>=H R<sub>2</sub>=OH

1 = GC-(4 $\alpha$ -8)-GC

2 = GC-(4 $\alpha$ -8)-EGC

3 = GC-(4 $\alpha$ -8)-GC-(4 $\alpha$ -8)-GC

Drug (conc.)	COX-1	COX-2
1 (10 $\mu$ M)	53,3 $\pm$ 3,8	64,4 $\pm$ 7,8
2 (10 $\mu$ M)	51,4 $\pm$ 6,5	65,6 $\pm$ 2,5
3 (10 $\mu$ M)	53,4 $\pm$ 11,7	65,1 $\pm$ 7,7
Extract (10 $\mu$ g/ml)	32,1 $\pm$ 5,6	64,8 $\pm$ 4,5

Results expressed as inhibition percentage of PGE2 production (table 1)

The model used for testing these prodelphinidins, namely the tridimensional culture of human chondrocytes allows chondrorepair to be quantified by the production of matrix substances: type II collagen, proteoglycans, and chondroresorption by the reduction in the levels of PGE2 and of OH° and O<sub>2</sub>° type free radicals produced [2]

Furthermore a selective inhibition of COX-2 over COX-1 was investigated.

Based on the using of a purified ovine enzyme test [3], we measured that a polyphenolic extract of *Ribes nigrum* leaves and prodelphinidins 1, 2 and 3, exhibited a greater inhibitor potency against COX-2 than on COX-1 (table 1).

### References

1. Tits, M., Angenot, L., Damas, J., Dierckxsens Y., Poukens P., (1991) *Planta Med.* 57 (Suppl.2): A 134
2. Franchimont, P.<sup>†</sup>, Bassleer, C., Angenot, L., Tits, M., (1997) N° Patent: US5670538: Use of prodelphinidins for obtaining medicaments intended for the treatment of arthrosis.
3. de Leval, X., Dogné, JM., Neven, P., Labasse, A., Delarge, J., Reginster, JY., Henrotin, Y., (1999) *J. Pharm. Belg.*, 54 (3): 89-90.