BRIEF COMMUNICATION

Inhibition of Angiogenesis by Oral Ingestion of Powdered Shark Cartilage in a Rat Model

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INTRODUCTION

The oral consumption of dried powdered shark cartilage has been widely promoted as a natural health remedy for the treatment of cancer (Wilson, 1994; Lane and Comac, 1992, 1996). It is proposed to act by preventing the angiogenesis required by solid tumours to grow larger than 2–3 mm (Folkman, 1995).

There is some evidence for the presence of anti-angiogenic factors in shark cartilage. Implantation of polymer pellets containing a shark cartilage extract alongside tumours in rabbit corneas inhibited tumour neovascularization (Lee and Langer, 1983). Injection of a suspension of shark cartilage reduced angiogenesis in tumours implanted in mice (Cataldi and Osbourne, 1995) and anti-angiogenic factors could be partially purified from shark cartilage (Oi-kawa et al., 1990). However, the links between oral ingestion of cartilage and its anti-angiogenic and anti-tumour properties have yet to be convincingly demonstrated.

Clinical trials of powdered shark cartilage as an anti-cancer agent have been initiated in Mexico and the United States but the results have yet to be published. In this study we have examined whether the oral ingestion of powdered shark cartilage by rats has any effect on the angiogenesis induced in mesenteric windows by mast cell stimulation.

MATERIALS AND METHODS

Shark cartilage. Dried powdered samples of cartilage from two commercial batches (designated A and B) manufactured principally from blue shark were supplied by McFarlane Laboratories Ltd. (Auckland, New Zealand).

Induced angiogenesis. A modification of the rat mesenteric-window assay (Norrby et al., 1990) was used. Sprague–Dawley rats (6 weeks old, equal numbers of male and female) were assigned to one of
TABLE 1
Percentage of Rat Mesenteric Window Area Occupied by Blood Vessels 16 and 25 Days after Stimulation with Compound 48/80

<table>
<thead>
<tr>
<th>Days after induction</th>
<th>Animal grouping</th>
<th>Diet</th>
</tr>
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<tbody>
<tr>
<td></td>
<td></td>
<td>Normal</td>
</tr>
<tr>
<td></td>
<td></td>
<td>n</td>
</tr>
<tr>
<td>16</td>
<td>All</td>
<td>52</td>
</tr>
<tr>
<td>16</td>
<td>Male</td>
<td>26</td>
</tr>
<tr>
<td>16</td>
<td>Female</td>
<td>26</td>
</tr>
<tr>
<td>25</td>
<td>All rats</td>
<td>80</td>
</tr>
<tr>
<td>25</td>
<td>Male</td>
<td>37</td>
</tr>
<tr>
<td>25</td>
<td>Female</td>
<td>43</td>
</tr>
</tbody>
</table>

Note. Each of the five groups comprised eight rats (four male and four female). Shark cartilage was administered at 6 g/kg of food. All data are means ± SEM. Statistical significance was assessed by Student’s t test. nd, not determined; n, number of windows.

RESULTS

Sixteen days after the commencement of Compound 48/80 administration, the percentage area that was vascularized in each mesenteric window from rats fed shark cartilage was significantly less than that in rats on an unsupplemented diet (Fig. 1, Table 1). Although Cartilage A appeared to be more effective than B, this difference was not statistically significant. A similar effect was seen 25 days after the commencement of stimulation (Table 1). At this time, Compound 48/80 was more effective at stimulating angiogenesis in female rats than in male rats.
FIG. 1—Continued
as previously reported (Norrby et al., 1990), but shark cartilage was as effective at reducing angiogenesis in males as in females.

There was a direct relationship between the inhibition of angiogenesis and the dose of Shark Cartilage A included in the rats’ diet up to an optimal level of 6 g/kg of food (Fig. 2).

**DISCUSSION**

These data demonstrate for the first time that the oral ingestion of powdered shark cartilage has a potent inhibitory effect on angiogenesis. The inhibitory factor must be stable in the gut and absorbed by the gastrointestinal tract in order for it to affect angiogenesis in the mesentery. This raises the question as to what is the likely identity of the inhibitory factor. The major components of powdered shark cartilage are protein (∼40%) and glycosaminoglycans (GAGs, ∼5–20%), with the remainder being principally calcium salts. Small portions of ingested proteins can cross the intestinal wall (Warshaw et al., 1974), but the majority will be digested to smaller peptides in the gut. However, GAGs, including chondroitin sulphate (Conte et al., 1995; Ronca and Conte, 1993), the major GAG present in cartilage, have been shown to be absorbed through the intestine largely intact when taken orally (Volpi, 1996). Work is continuing to determine which of the components of shark cartilage is responsible for the orally available antiangiogenic activity observed here.

**REFERENCES**


