

A Weck-Cel micro sponge 2x2x2 mm in size (Weck, Research Triangle Park, N.C.) was saturated with 100 μ L of either BSS PLUS® (Alcon), mitomycin C (0.5 mg/mL in BSS PLUS®), or test article and placed for 5 minutes between the conjunctiva and sclera to cover the appropriate area of the planned filtration site. The conjunctival wound was then rinsed with about 25 mL of BSS PLUS®. This process was immediately followed by a clear corneal paracentesis, a 2 mm sclerectomy, and an iridectomy. The corneal paracentesis was used to administer 1 mL of a surgical irrigation solution (e.g., BSS PLUS® or COMPOUND D TIS) into the anterior chamber for washing and removal of excess control or test agent administered to the subconjunctival wound. The corneal paracentesis site was also used to administer COMPOUND D, as described above, supplemented PROVISC® (Alcon) composition of the present invention (0.3 mL) to replace the aqueous humor. The conjunctival wound was then closed with 9-0 sutures.

Each study group consisted of 6 animals and received treatment as described in Table 1 below:

TABLE 1

| Summary of Glaucoma Filtration Surgery Experimental Treatment Groups | | | |
|---|---|--------------------------------|---------------------------------------|
| Study Group | Conjunctival Wound Treatment (sponge) | Anterior Chamber Irrigation | Anterior Chamber Fluid Replacement |
| I | BSS PLUS® | BSS PLUS® | BSS PLUS® |
| II | Mitomycin C† | BSS PLUS® | BSS PLUS® |
| III | COMPOUND D TIS§ | COMPOUND D TIS | COMPOUND D- PROVISC®‡ |
| IV | Mitomycin C | COMPOUND D TIS | COMPOUND D- PROVISC® |

†0.5 mg/mL in BSS PLUS®

§Therapeutic Irrigation Solution consisting of BSS PLUS® supplemented with COMPOUND D (0.5 μ M) and cremophor EL (0.05%)

‡PROVISC® supplemented with COMPOUND D (0.5 μ M) and cremophor EL (0.05%)

Postoperative assessment of bleb vascularity was conducted with conscious animals. Measurement of bleb size was carried out under general anesthesia (ketamine HCl/xylazine). Routine post-surgical examinations were conducted on days 1, 3, 5, 10, and 14 and every week thereafter until the time of bleb failure. Bleb failure was defined as a bleb score value of zero where the bleb score represents the sum of bleb size and height.

The number of functioning blebs through 8 weeks is reported in Table 2, below:

TABLE 2

| Study Group | Number of Functioning Blebs Post Operative Week | | | |
|-------------|--|-------|-------|-------|
| | 1 wk | 2 wks | 4 wks | 8 wks |
| I | 0/6 | 0/6 | — | — |
| II | 6/6 | 6/6 | 6/6 | 4/6 |
| III | 6/6 | 2/6 | 1/6 | — |
| IV | 6/6 | 6/6 | 6/6 | 6/6 |

EXAMPLE 2

The following is an example of a preferred composition of the present invention:

| Ingredient | % w/v |
|--|-------------|
| Compound D | 0.000023 |
| Cremophor EL | 0.05 |
| Hyaluronic Acid, Sodium Salt | 1 |
| Dibasic Sodium Phosphate (Anhydrous) | 0.056 |
| Monobasic Sodium Phosphate (Monohydrate) | 0.004 |
| Sodium Chloride | 0.84 |
| Hydrochloric Acid | pH adjusted |
| Sodium Hydroxide | pH adjusted |
| Water | QS |

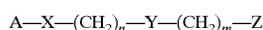
EXAMPLE 3

The following is an example of a viscoelastic composition of the present invention wherein "Compound" denotes a compound of the present invention:

| Ingredient | % w/v |
|--|----------------|
| Compound | 0.00001–0.0010 |
| Cremophor EL | 0.05 |
| Sodium Chondroitin Sulfate | 4.0 |
| Sodium Hyaluronate | 3.0 |
| Sodium Dihydrogen Phosphate, Monohydrate | 0.045 |
| Disodium Hydrogen Phosphate, Anhydrous | 0.2 |
| Sodium Chloride | 0.310 |
| Water | QS |
| Hydrochloric Acid | pH adjusted |
| Sodium Hydroxide | pH adjusted |

What is claimed is:

1. A viscoelastic composition comprising a pharmaceutically acceptable viscoelastic vehicle and an amount of a compound of the following formula effective to decrease inflammation, free radical/oxidative damage or cellular proliferation in mammalian tissues;



wherein:

A is a non-steroidal anti-inflammatory agent originally having a carboxylic acid moiety;

X is O or NR;

A—X is an ester or amide formed from the carboxylic acid moiety and the X;

R is H, C₁–C₆ alkyl or C₃–C₆ cycloalkyl;

Y, if present, is O, NR, C(R)₂, CH(OH) or S(O)_n;

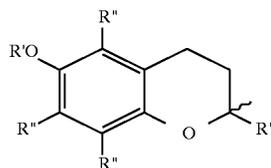
n is 2 to 4 and m is 1 to 4 when Y is O, NR, or S(O)_n;

n is 0 to 4 and m is 0 to 4 when Y is C(R)₂ or is not present;

n is 1 to 4 and m is 0 to 4 when Y is CH(OH);

n' is 0 to 2; and

Z is selected from the group consisting of:



a