

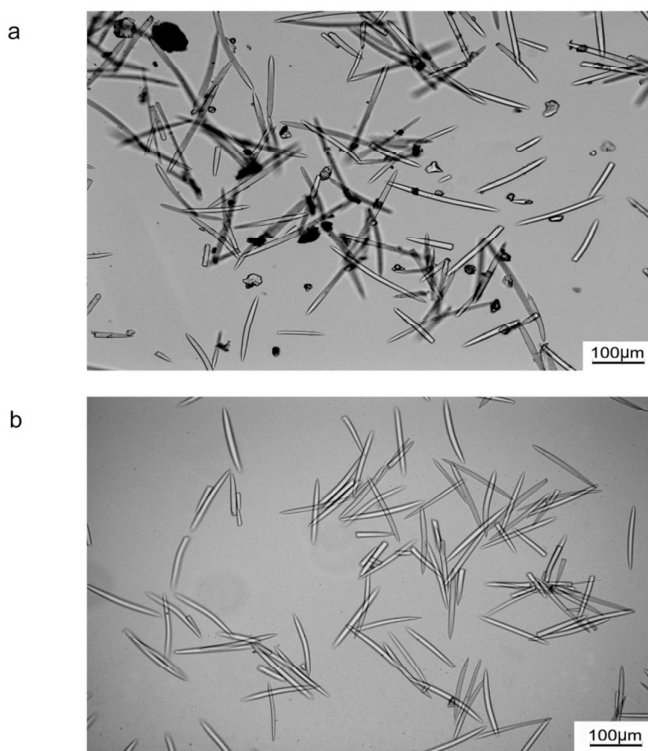
Supporting Information

# Skin delivery of hydrophilic biomacromolecules using marine sponge spicules

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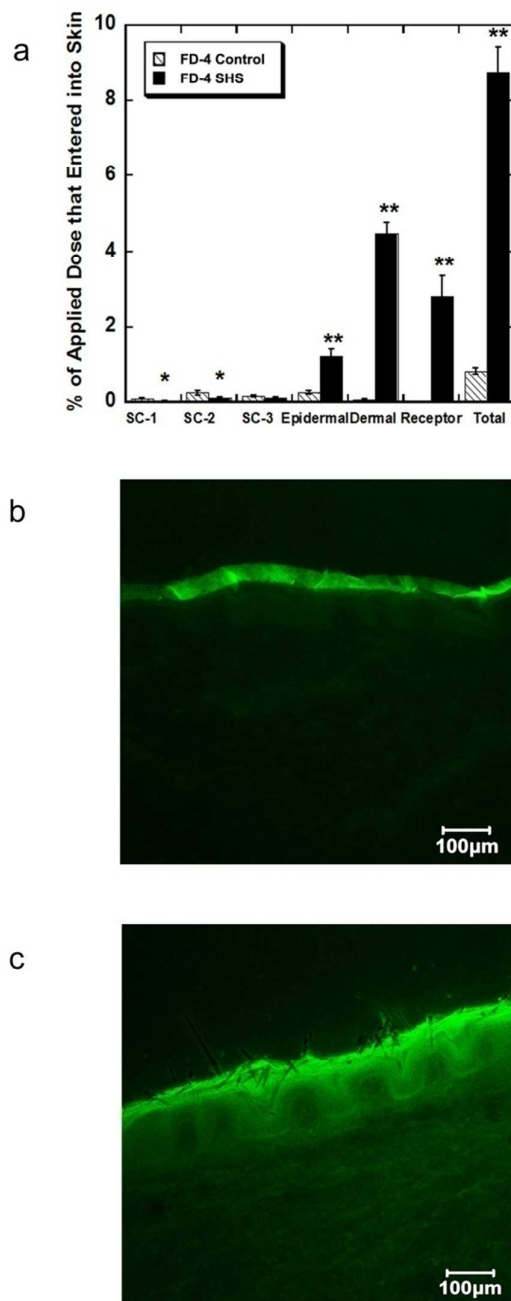
Dexiang Wang and Ming Chen

Figure S1



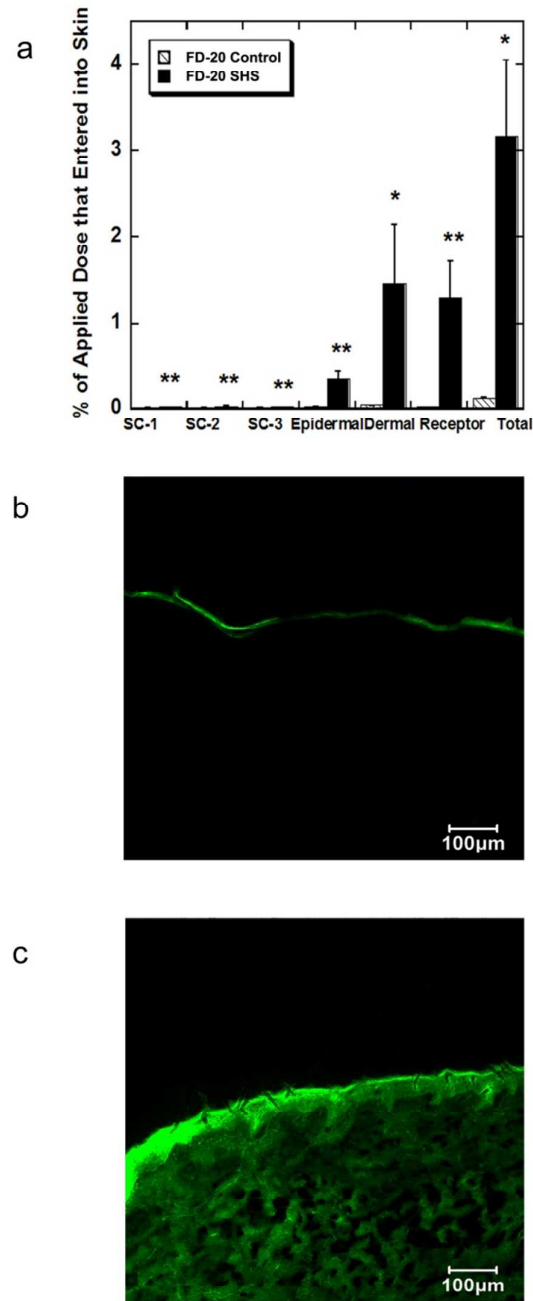
**Fig. S1** Purification of SHS. **(a)** Unpurified SHS. **(b)** Purified SHS.

**Figure S2**



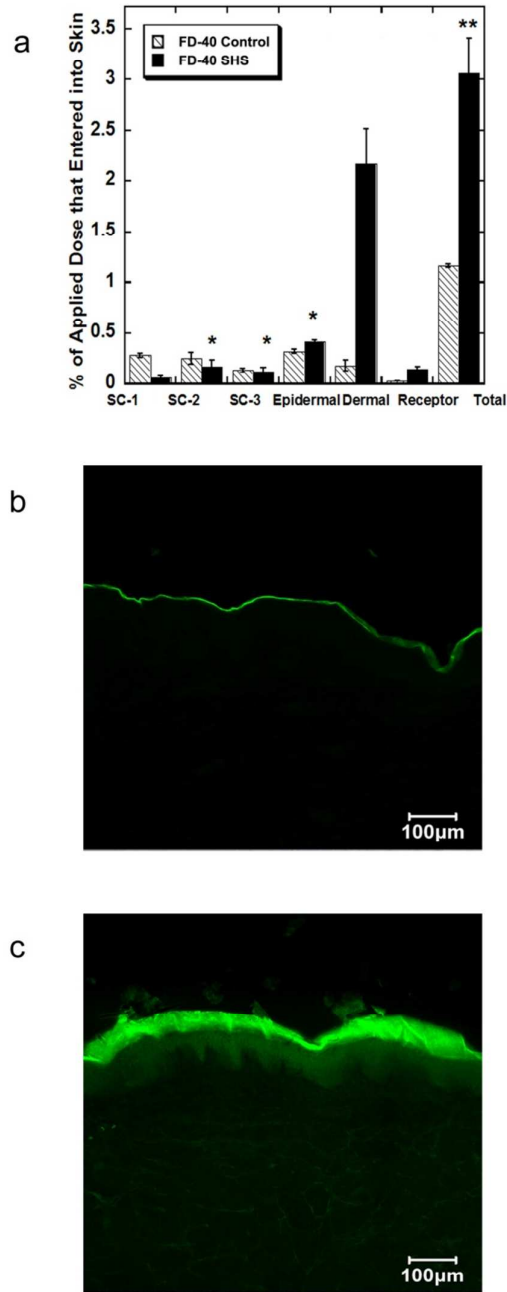
**Fig. S2** SHS topical application enhanced penetration of FD-4 in porcine skin *in vitro*. **(a)** Skin penetration and distribution profile of FD-4. Solid black bars: SHS with a dose of 10 mg per 1.77 cm<sup>2</sup> using S-massage mode for 120 seconds; Backslash bars: control group; **(b)** Confocal image of skin penetration of FD-4 from control group; **(c)** Confocal image of skin penetration of FD-4 with SHS treatment. Values represent mean  $\pm$  SD (n=3). \*Statistically was different from control group ( $p < 0.05$ ). \*\*Statistically very different from control group ( $p < 0.01$ ).

**Figure S3**



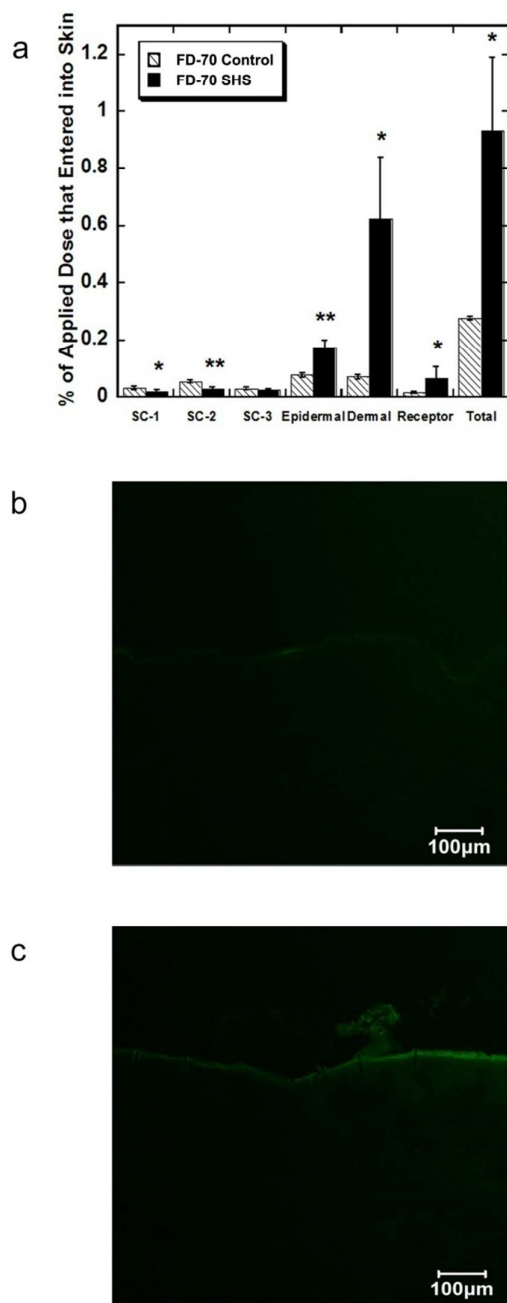
**Fig. S3** SHS topical application enhanced penetration of FD-20 in porcine skin *in vitro*. **(a)** Skin penetration and distribution profile of FD-20. Solid black bars: SHS with a dose of 10 mg per 1.77 cm<sup>2</sup> using S-massage mode for 120 seconds; Backslash bars: control group; **(b)** Confocal image of skin penetration of FD-20 from control group; **(c)** Confocal image of skin penetration of FD-20 with SHS treatment. Values represent mean  $\pm$  SD (n=3). \*Statistically was different from control group ( $p < 0.05$ ). \*\*Statistically very different from other group ( $p < 0.01$ ).

**Figure S4**



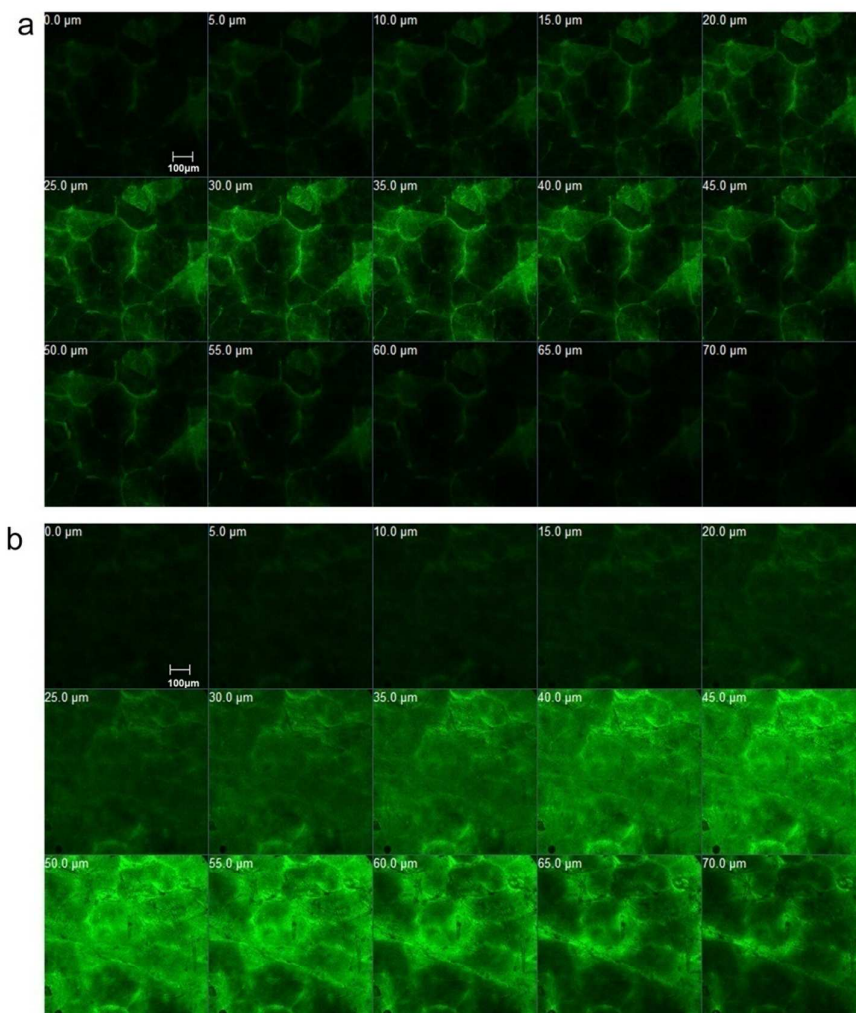
**Fig. S4** SHS topical application enhanced penetration of FD-40 in porcine skin *in vitro*. **(a)** Skin penetration and distribution profile of FD-40. Solid black bars: SHS with a dose of 10 mg per 1.77 cm<sup>2</sup> using S-massage mode for 120 seconds; Backslash bars: control group; **(b)** Confocal image of skin penetration of FD-40 from control group; **(c)** Confocal image of skin penetration of FD-40 with SHS treatment. Values represent mean  $\pm$  SD (n=3). \*Statistically was different from other group ( $p < 0.05$ ). \*\*Statistically very different from other group ( $p < 0.01$ ).

**Figure S5**



**Fig. S5** SHS topical application enhanced penetration of FD-70 in porcine skin *in vitro*. **(a)** Skin penetration and distribution profile of FD-70. Solid black bars: SHS with a dose of 10 mg per 1.77 cm<sup>2</sup> using S-massage mode for 120 seconds; Backslash bars: control group; **(b)** Confocal image of skin penetration of FD-70 from control group; **(c)** Confocal image of skin penetration of FD-70 with SHS treatment. Values represent mean  $\pm$  SD (n=3). \*Statistically was different from other group ( $p < 0.05$ ). \*\*Statistically very different from other group ( $p < 0.01$ ).

**Figure S6**



**Fig. S6** Penetration and distribution of FD-10 into skin by confocal scanograms. **(a)** Superficial distribution of FD-10 in porcine skin of control group. **(b)** Deep penetration and homogeneous distribution of FD-10 into skin deep layer with SHS treatment.