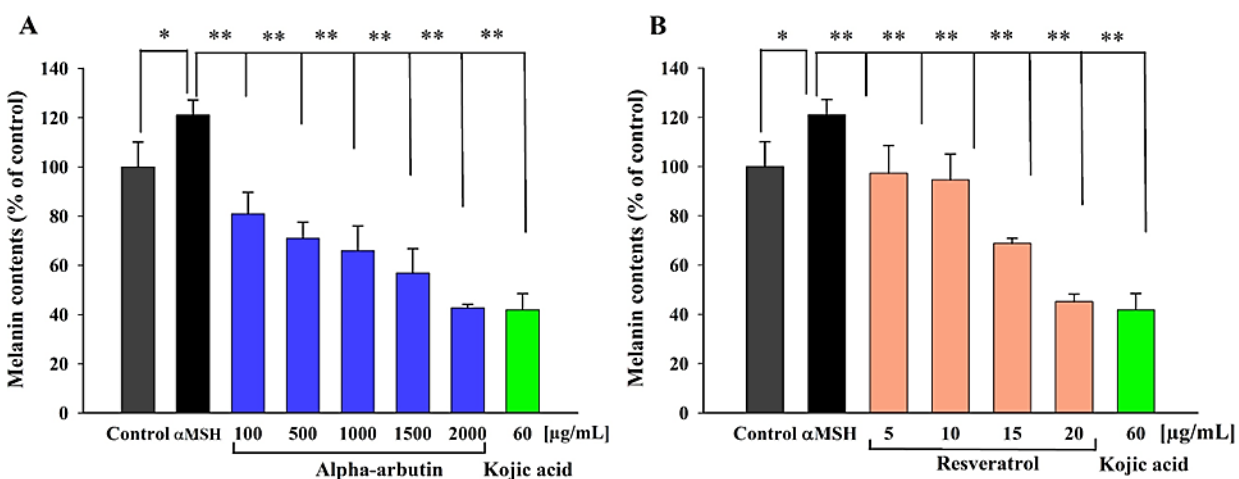
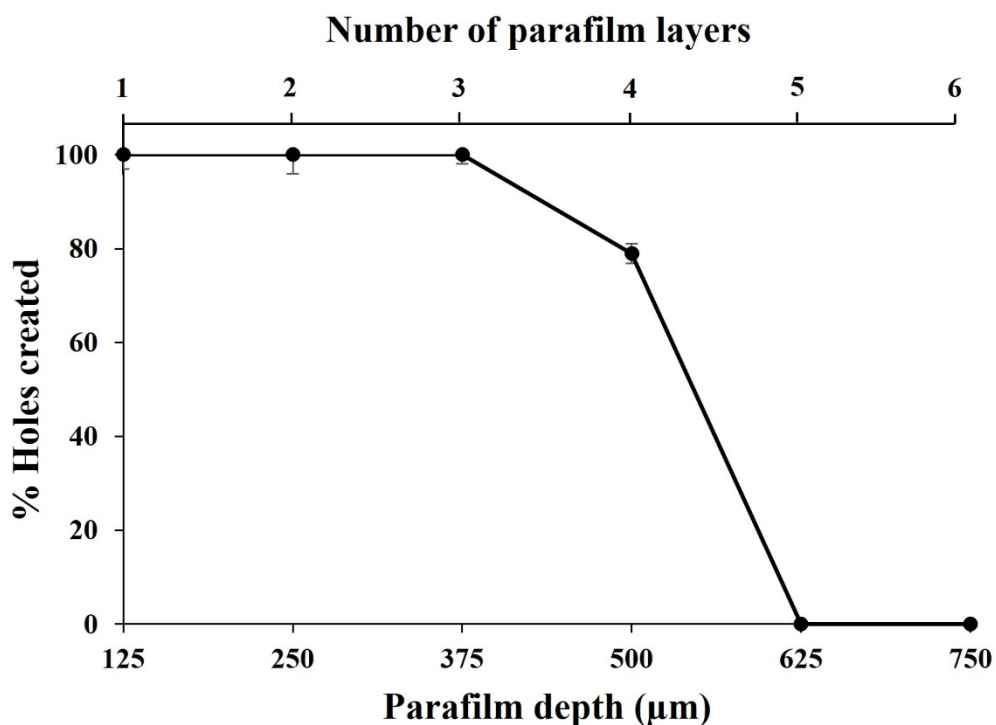


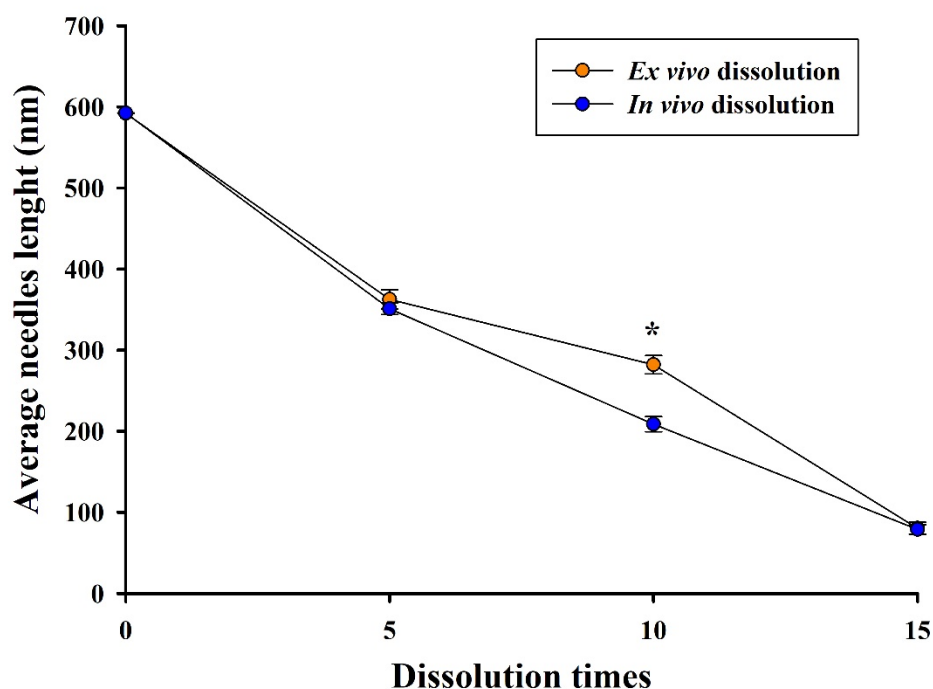
## Supplementary material



**Fig. s1.** Effects of different concentrations of (C) AA and (D) Res on melanin production in B16F10 melanoma cells induced with  $\alpha$ -MSH (\* $P$  < 0.05 vs. control, \*\* $P$  < 0.01 vs.  $\alpha$ -MSH induced group,  $n$  = 3).



**Fig. s2.** Percentage of holes created in each parafilm layer after the application of F3 DMN patches with a 10.769 N/patch insertion force for 30 s (means  $\pm$  SD,  $n$  = 3).



**Fig. s3.** Dissolution profiles of DMN patches (F3) at different time points when applied *ex vivo* (●) and *in vivo* (●) (\* $P < 0.05$  compared with *in vivo*).

**Table s1.** CI analyses of melanin content in B16F10 melanoma cells treated with different AA concentrations AA at a fixed Res concentration or different Res concentrations at a fixed AA concentration for 48 h.

| Concentrations (µg/mL) |         | AA:Res ratios | CI value* |
|------------------------|---------|---------------|-----------|
| AA                     | Fix Res |               |           |
| 20                     | 20      | 1:1           | 0.96      |
| 100                    | 20      | 5:1           | 0.85      |
| 500                    | 20      | 25:1          | 0.74      |
| 1000                   | 20      | 50:1          | 0.77      |
| 1500                   | 20      | 75:1          | 0.74      |
| 2000                   | 20      | 100:1         | 0.21      |
| 3000                   | 20      | 150:1         | 0.13      |
| Concentrations (µg/mL) |         | AA:Res ratios | CI value* |
| Fix AA                 | Res     |               |           |
| 2000                   | 5       | 400:1         | 1.96      |
| 2000                   | 10      | 200:1         | 1.13      |
| 2000                   | 15      | 133:1         | 0.45      |

|      |    |       |      |
|------|----|-------|------|
| 2000 | 20 | 100:1 | 0.22 |
| 2000 | 25 | 80:1  | 0.20 |
| 2000 | 30 | 67:1  | 0.19 |

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\*CI<1 means synergism, CI>1 means antagonism