Two kinds of cosmetic formulations approach to skin-whitening through multiple mechanisms in vitro and in vivo

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Introduction:

Among Chinese women, the proportion of people with stains can be as high as 98%. This is a huge data. More and more beauty lovers join this "battle" against stains, so more and more Anti-freckle and spot-lightening products have entered the market, but effective and safe multi-channel suppression products urgently need to be developed. The whitening mechanism mainly includes:

1) Inhibit the transcription of genes in melanin synthesis-related enzymes.
2) Inhibit the synthesis of melanin,tyrosinase is the rate-limiting enzyme in the melanin synthesis pathway.
3) Inhibit the transport of melanosomes, the protease-active receptor 2 (PAR-2) is the main regulator of melanosome transport on the surface of the keratinocyte membrane.
4) Reduce active oxygen free radicals

Many topical products are commercially available proposed to alleviate hyperpigmentation but only contain tyrosinase inhibitors. Therefore, we aim to develop 2 formulas of the active ingredients, which act on multiple targets and core signaling pathways to achieve skin-whitening effects.

Materials & Methods:

Research approach

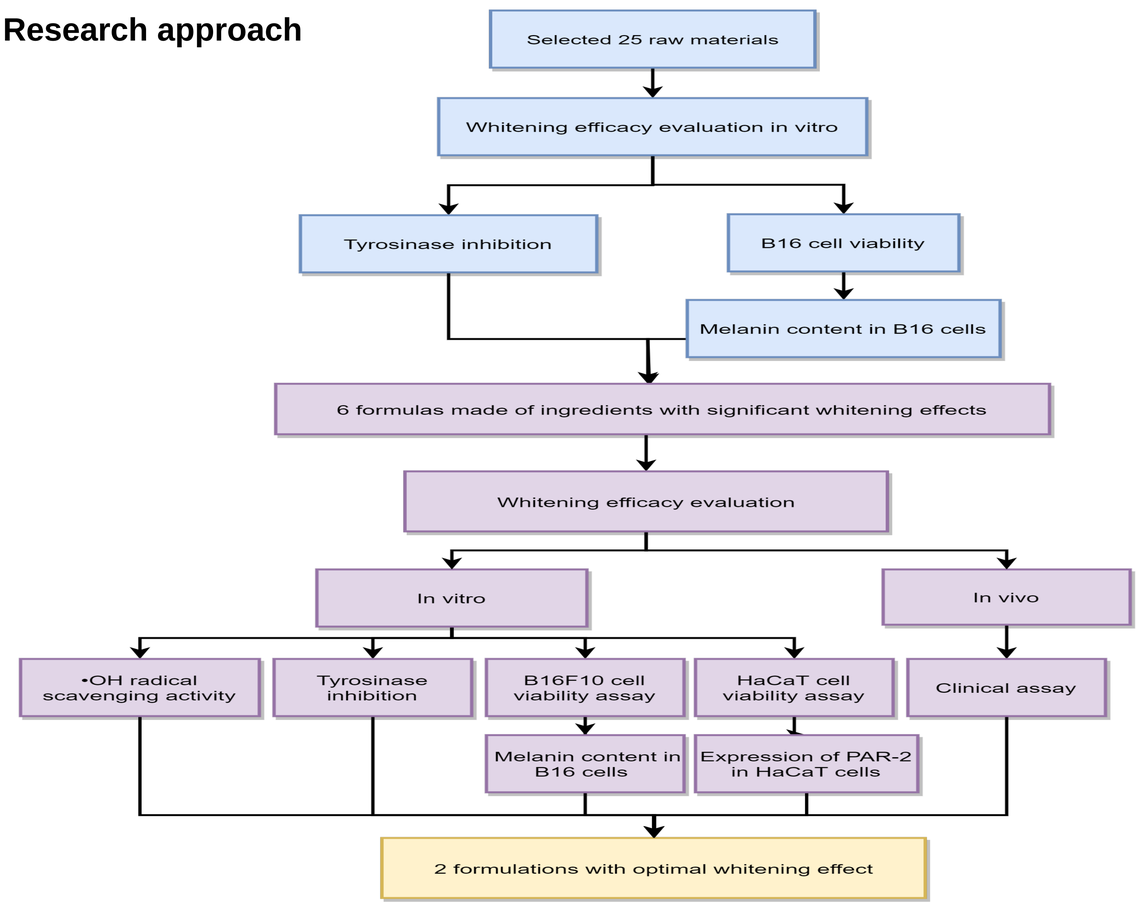

Fig.1 Methods flow chart.

Formulas

Table 1 Composition of 6# formula freeze-dried powder

Ingredient	Content%(w/w)
yeast/rice fermentation filtrate	20
nicotinamide	5
tranexamic acid	10
ascorbyl glucoside	1
palmitoyl tripeptide-5	10 μg/ml
palmitoyl tetrapeptide-7	10 μg/ml
α-arbutin	5

Table 2 Composition of 7# formula freeze-dried powder

Ingredient	Content%(w/w)
yeast/rice fermentation filtrate	20
nicotinamide	5
tranexamic acid	10
ascorbyl glucoside	1
nonapeptide-1	10 μg/ml
palmitoyl tripeptide-5	10 μg/ml
palmitoyl tetrapeptide-7	10 μg/ml
α-arbutin	5

Table 3 Composition of 9# formula freeze-dried powder

Ingredient	Content%(w/w)
yeast/rice fermentation filtrate	20
nicotinamide	5
tranexamic acid	10
ascorbyl glucoside	1
nonapeptide-1	3~10 μg/ml
potassium methoxysalicylate	5
α-arbutin	5

Table 4 Composition of 10# formula freeze-dried powder

Ingredient	Content%(w/w)
yeast/rice fermentation filtrate	20
nicotinamide	5
tranexamic acid	10
ascorbyl glucoside	1
palmitoyl tripeptide-5	10 μg/ml
potassium methoxysalicylate	5
α-arbutin	5

Table 5 Composition of 11# formula freeze-dried powder

Ingredient	Content%(w/w)
aloe yohjyu matsu ekisu	20
nicotinamide	5
tranexamic acid	10
ascorbyl glucoside	1
nonapeptide-1	10 μg/ml
α-arbutin	5

Table 6 Composition of 12# formula freeze-dried powder

Ingredient	Content%(w/w)
chrysanthelum indicum extract	20
nicotinamide	5
tranexamic acid	10
ascorbyl glucoside	1
nonapeptide-1	10 μg/ml
α-arbutin	5

Results & Discussion:

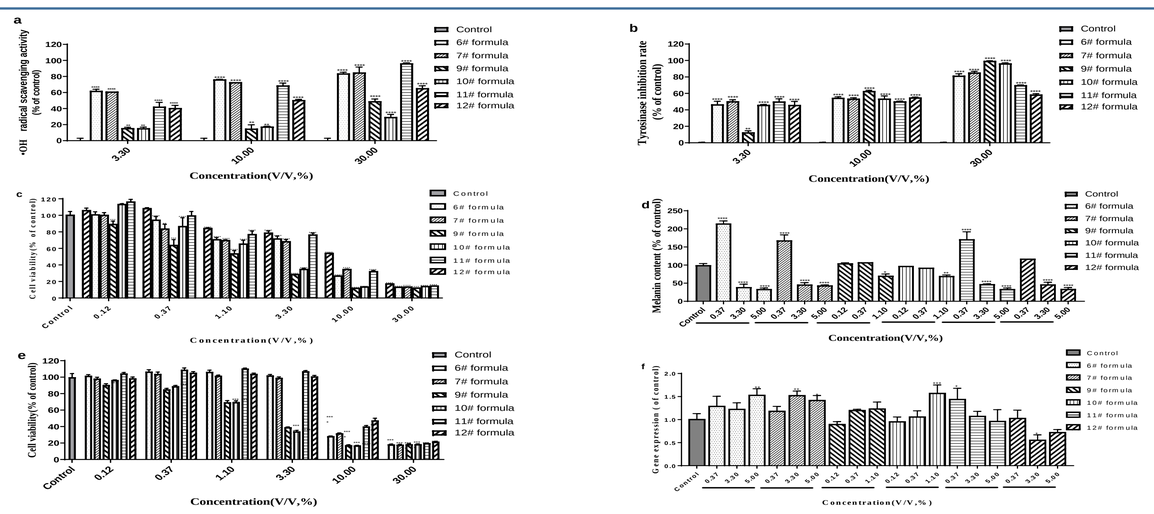

Fig.2 Biological activity of selected 6 formulas. a. •OH radical scavenging activity; b. the inhibition of tyrosinase activity; c. B16 cell viability; d. Melanin content; e. HaCaT Cell viability; f. Expression of PAR-2 of 6 formulas in HaCaT cells. *P < 0.05; **P < 0.01; *** P < 0.001; ****P < 0.0001 compared to control.

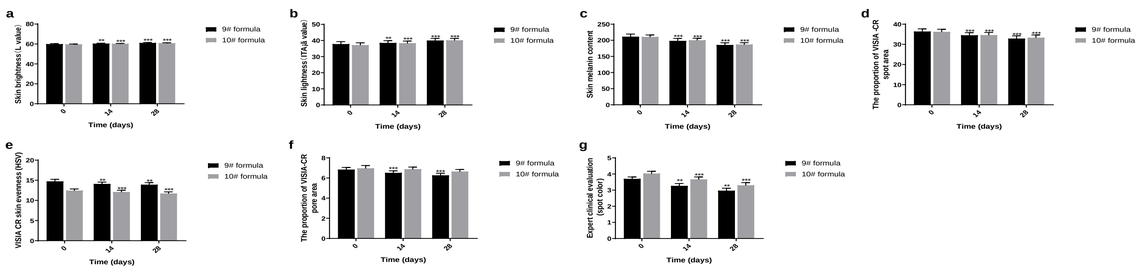

Fig.3 Clinical data of 9# and 10# formulas. *P < 0.05; **P < 0.01; *** P < 0.001; ****P < 0.0001 compared to 0 day.

All six formulas had significant •OH radical scavenging activity(Fig 2a).

The 9# and 10# formulas showed significant whitening activity in terms of tyrosinase inhibition(Fig 2b), intracellular melanin content(Fig 2d) and human clinical trials(Fig 3).

The 9# and 10# formulas can promote the expression of PAR-2 in HaCaT cells(Fig 2f).

Above all, the present in vitro and in vivo data proved that 9# and 10# formulas we developed were effective approach to skin-whitening through multiple targets

Conclusions:

With the surge in demand for whitening products, it has become increasingly important that cosmetics can be used as powerful and safe whitening products through multiple mechanisms.

In this study, through in vitro tyrosinase inhibition experiment and B16 cell safety and melanin content experiment, several raw materials with good safety tyrosinase inhibition effect are screened, such as astaxanthin, aloe leaf juice, palmitoyl tetrapeptide-7, α-arbutin (1), α-arbutin (2), chamomile extract, 4MSK, salidroside, resveratrol, palmitoyl tripeptide-5, oligopeptide-1, tripeptide-1, GSH, and nicotinamide which can inhibit melanin transfer by inhibiting PAR-2 mRNA expression.

6 freeze-dried powder formulas were made from the raw materials screened above, and further efficacy evaluation experiments were carried out. The present in vitro and in vivo data proved that 9# and 10# formulas we developed were effective approach to skin-whitening through multiple mechanisms. The resulting clinical improvement of skin hyperpigmentations revealed the selected 2 formulas as very safe and valuable active products for the management of pigmentation disorders.

Aknowledgments:

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