

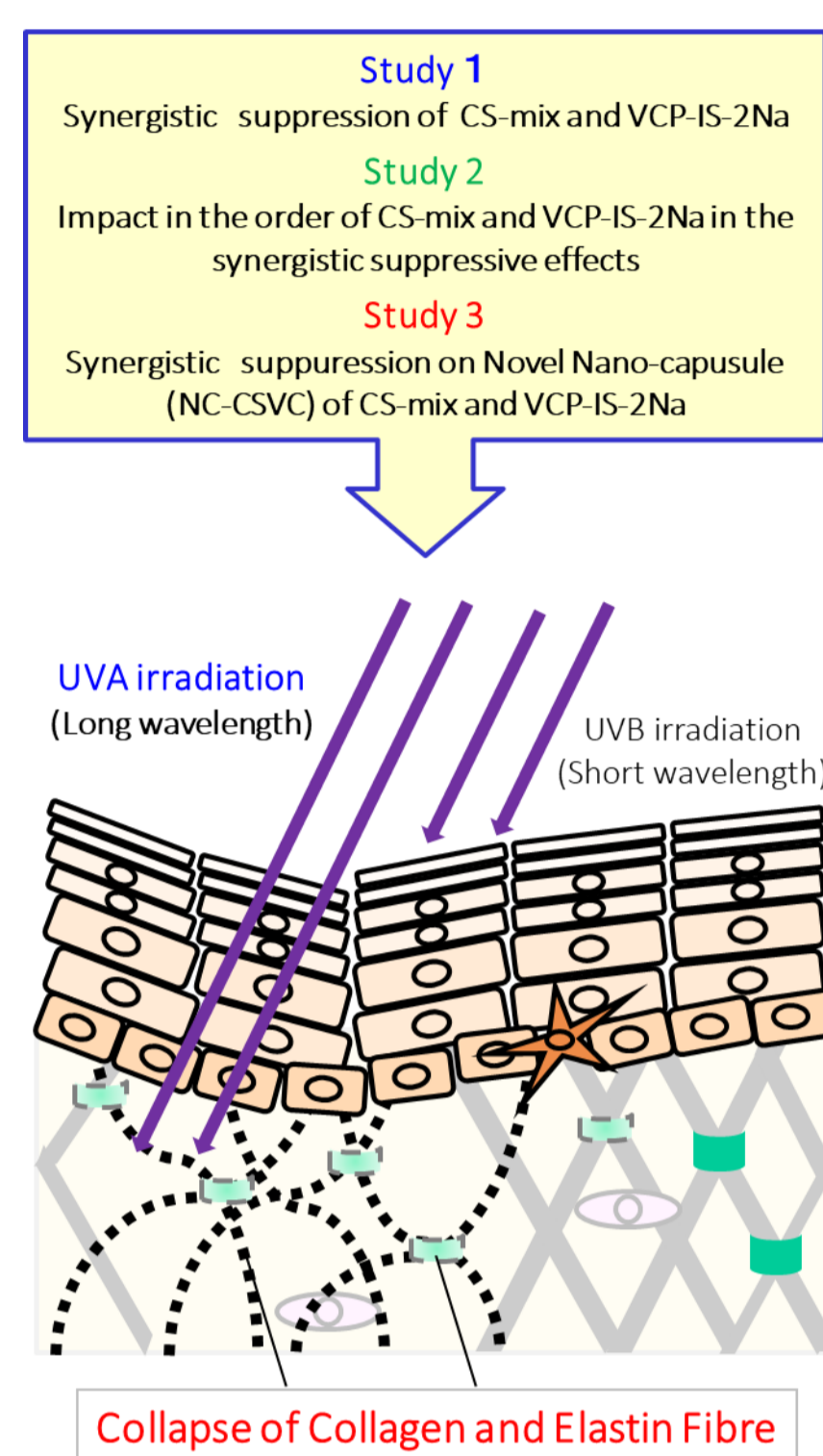
# Nano-capsules of naturally occurring phenylpropanoids and an amphiphilic vitamin C derivative provide synergistic protection against UVA irradiation-induced skin damage and collagen / elastin fibre reconstruction

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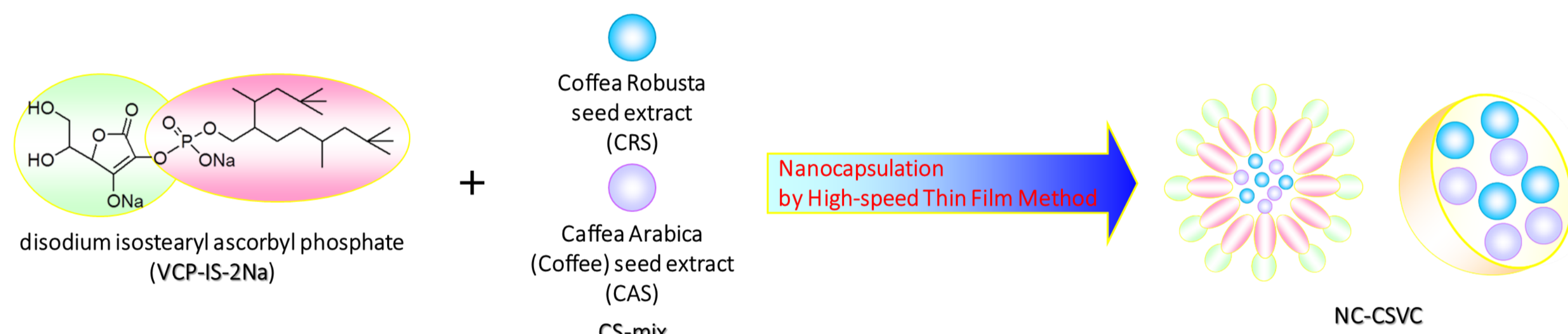
## Introduction:

We have been reported that the mix extract (CS-mix), Coffea Robusta seed extract (CRS) and Coffea Arabica (Coffee) seed extract (CAS), which contains many amounts of caffeic acid and chlorogenic acid, prevented UVA irradiation-induced decreased levels of collagen synthesis and increased level of pro-MMP-1 production [1]. Furthermore, CRS and CAS suppressed the decreases of the mRNA expression of microfibril-related genes exposed to UVA irradiation. Therefore, we developed a nano-capsule (NC-CS) containing CRS and CAS by polyglyceryl fatty derivative. NC-CS had greater suppressive potencies against the decrease in collagen, the MMP-1 production, and the downregulation of the mRNA expression of microfibril-related genes induced by UVA irradiation on NHDFs. We have recently synthesized an amphiphilic ascorbic derivative, disodium isostearyl ascorbyl phosphate (VCP-IS-2Na), which exhibited high stability in various aqueous solutions at a wide range of pH values and satisfactory thermal stability [2]. VCP-IS-2Na has skin permeability superior to that of VC and exhibits VC activity in vitro and in vivo after enzymatic hydrolysis to free VC by phosphatase and/or esterase. So far, we have shown that VCP-IS-2Na has anti-melanogenesis effects [3] and stimulation on collagen synthesis [4]. In this study, we investigated whether the combination of CS-mix and VCP-IS-2Na exerted a synergistic suppressive effect on collagen synthesis, MMP-1 activity, mRNA expression of microfibril-relating genes in normal human dermal fibroblasts (NHDFs) under UVA irradiation. Furthermore, we also examined whether nanoencapsulation of CS-mix with VCP-IS-2Na enhanced its effect in human skin models.

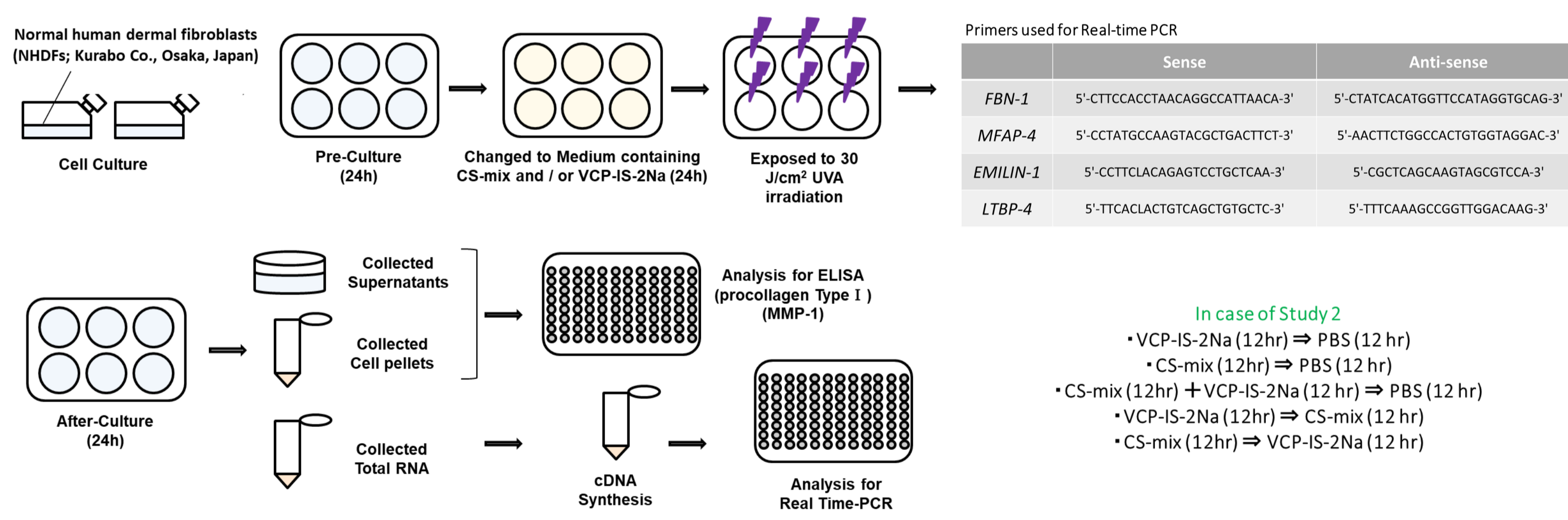


## Materials & Methods:

### Prepare of Nano-capsule CSVC (NC-CSVC)



### Evaluation of CS-mix and VCP-IS-2Na on suppression against UVA-irradiation skin damage and collagen reconstruction in normal human dermal fibroblasts (NHDFs)



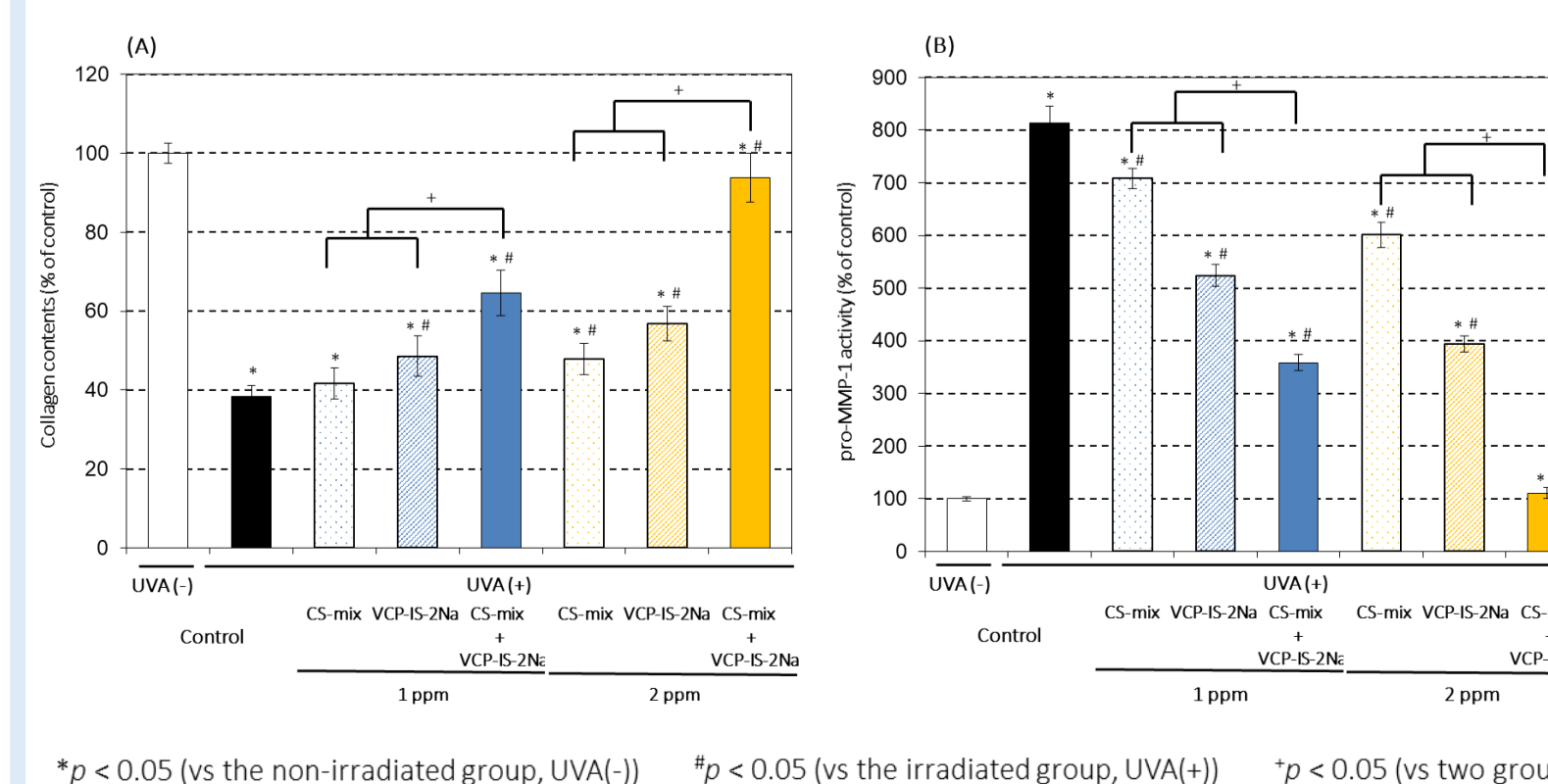
### Evaluation of NC-CSVC on suppression against UVA-irradiation skin damage and collagen reconstruction and skin permeation in reconstructed human skin model (EPI-200X)



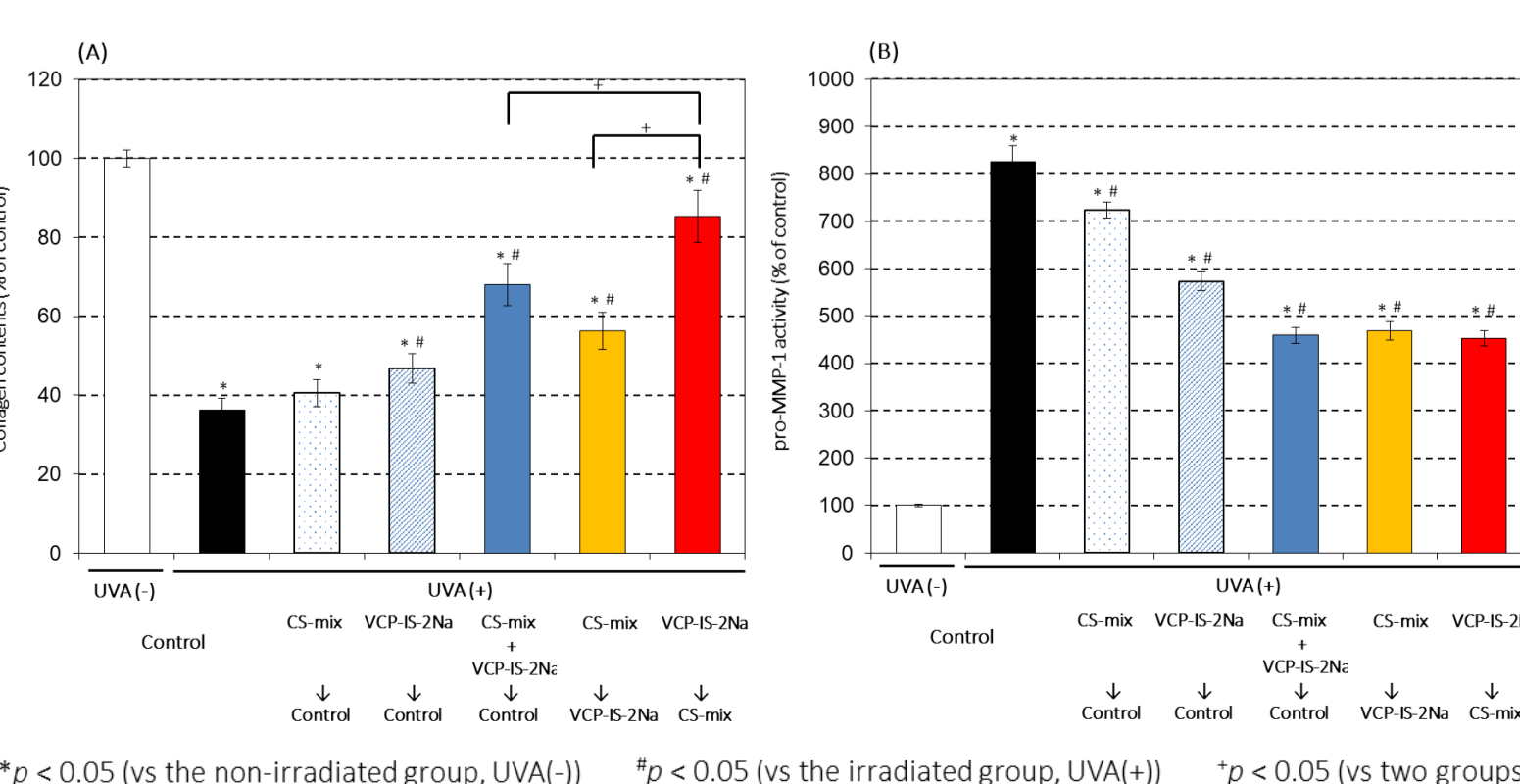
## Results & Discussion:

### Collagen synthesis and pro-MMP-1 activity

**Study 1**  
Suppressive effect of CS-mix and VCP-IS-2Na on collagen decrease (A) and MMP-1 production (B) stimulated by UVA irradiation in NHDFs



**Study 2**  
Impact in the order of CS-mix and VCP-IS-2Na in the synergistic effects on collagen decrease (A) and MMP-1 production (B)

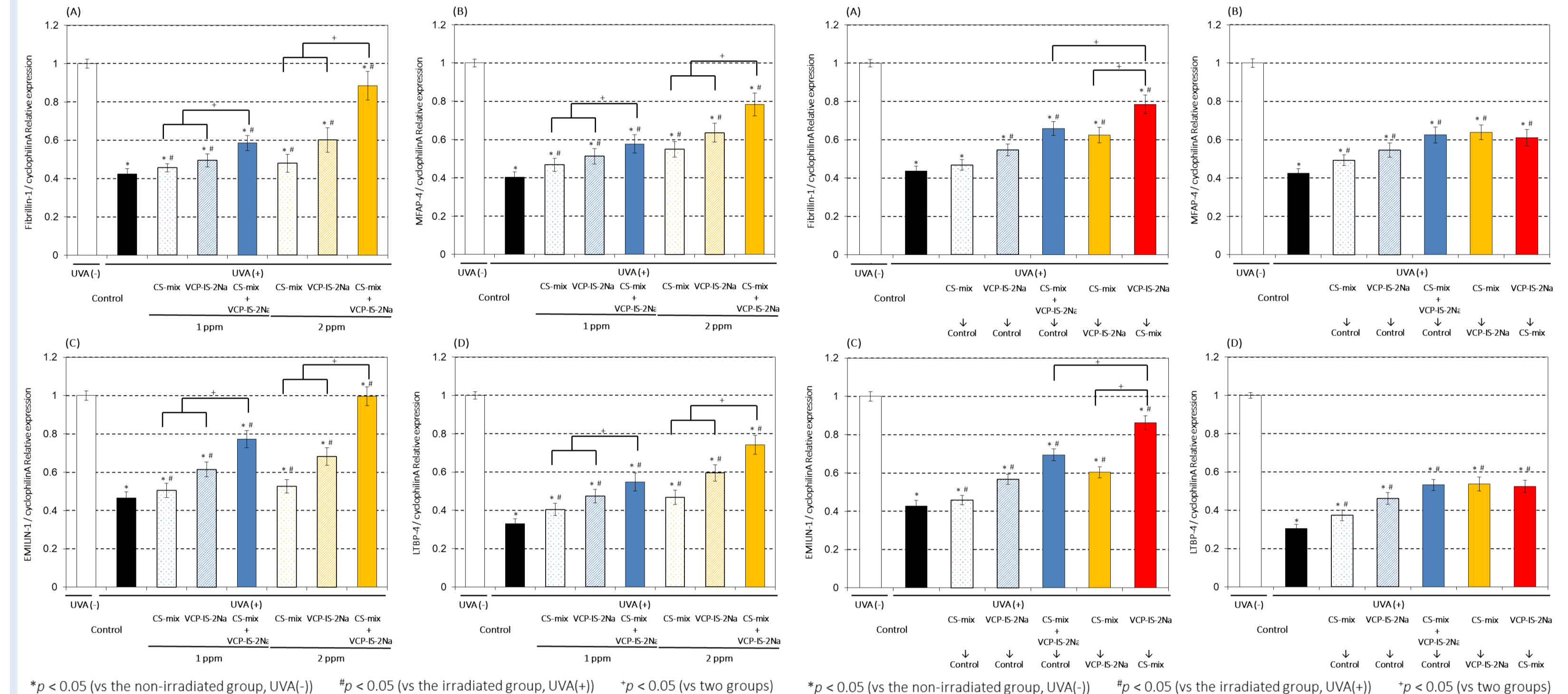


- ◆ The combination of CS-mix and VCP-IS-2Na efficiently synergistically protected against the decrease in type I collagen production, the excess production of MMP-1.
- ◆ Approach with VCP-IS-2Na to NHDFs first and then with CS-mix is more effective on synergistic activity.

## Results & Discussion:

### mRNA expression of microfibril-relating genes

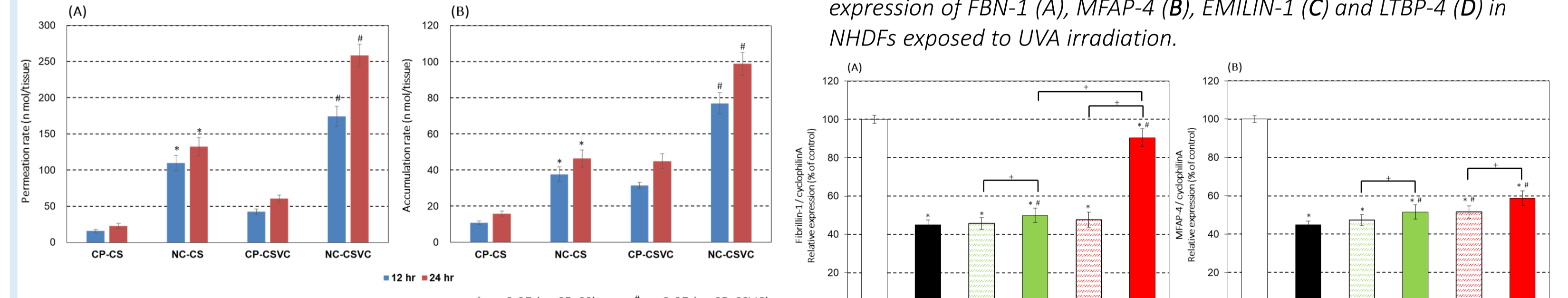
**Study 1**  
Suppressive effect of CS-mix and VCP-IS-2Na on the downregulation of the mRNA expression of FBN-1 (A), MFAP-4 (B), EMILIN-1 (C) and LTBP-4 (D) in NHDFs exposed to UVA irradiation.



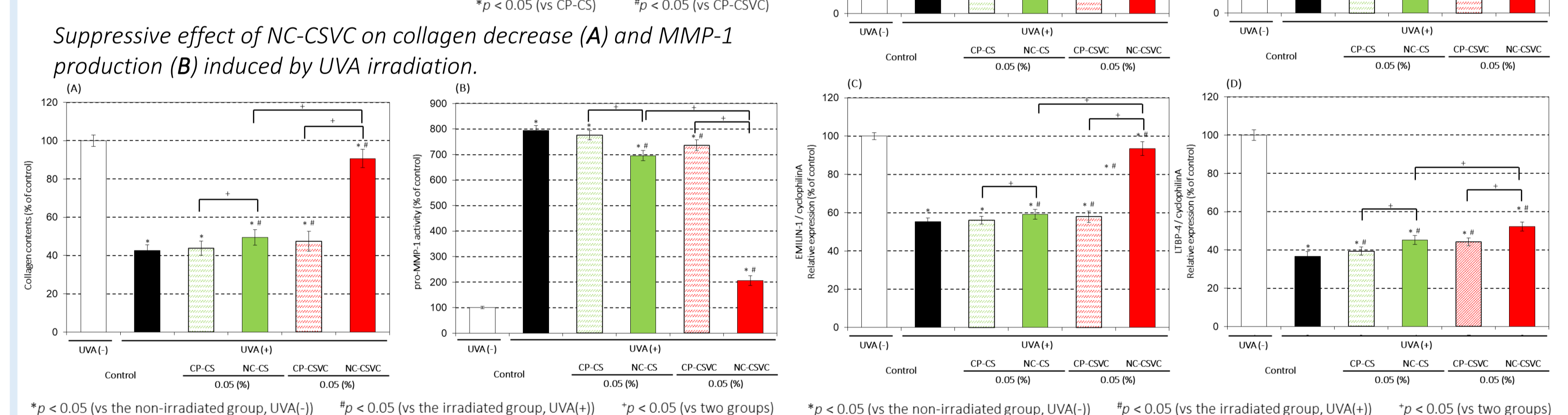
**Study 2**  
Suppressive effect of CS-mix and VCP-IS-2Na on the downregulation of the mRNA expression of FBN-1 (A), MFAP-4 (B), EMILIN-1 (C) and LTBP-4 (D) with changing the processing order of the samples.

- ◆ Combination of CS-mix and VCP-IS-2Na efficiently synergistically protected against the downregulation of FBN-1 and EMILIN-1.
- ◆ Approach with VCP-IS-2Na to NHDFs first and then with CS-mix is more effective on synergistic activity.

**Study 3**  
Skin permeation (A) and accumulation (B) of NC-CSVC on EPI-200X.



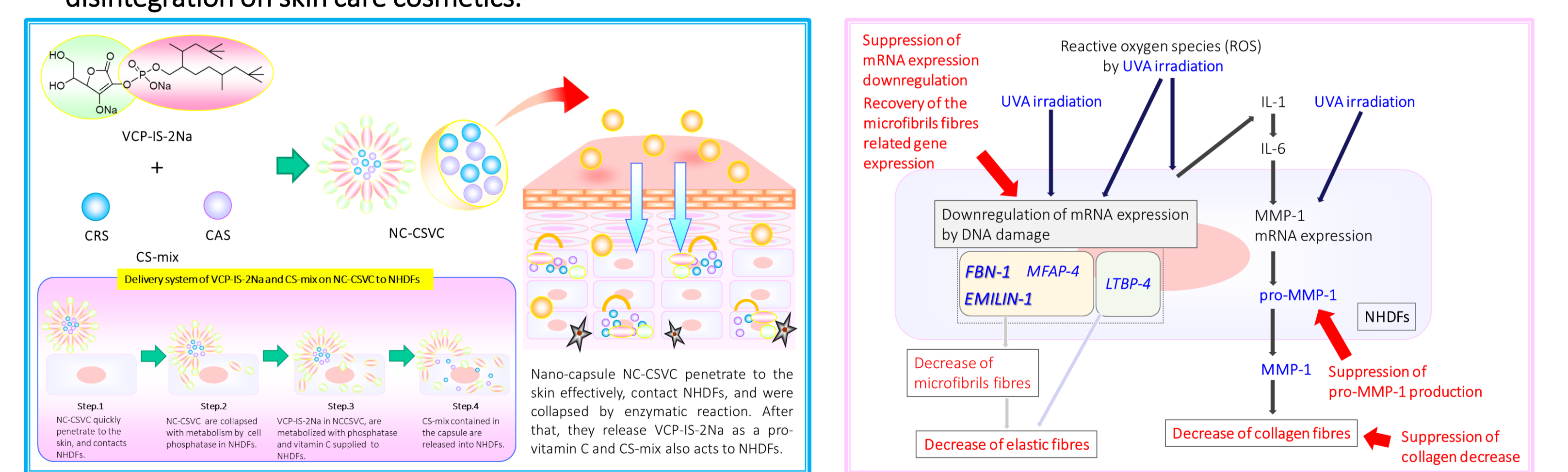
Suppressive effect of NC-CSVC on the downregulation of the mRNA expression of FBN-1 (A), MFAP-4 (B), EMILIN-1 (C) and LTBP-4 (D) in NHDFs exposed to UVA irradiation.



- ◆ NC-CSVC efficiently synergistically protected more multiples in permeation power on collagen synthesis, MMP-1 activity, mRNA expression of microfibril-relating genes than CP-CSVC.

## Conclusions:

- ◆ The combination of CS-mix and VCP-IS-2Na efficiently synergistically protected against the decrease in type I collagen production, the excess production of MMP-1 and the downregulation of FBN-1 and EMILIN-1.
- ◆ A novel nano-capsule NC-CSVC realized the component treatment to NHDFs in an appropriate order by transdermal enzymatic delivery system, and is effective as a method for maximizing these synergistic effect.
- ◆ Combination of CS-mix and VCP-IS-2Na and NC-CSVC may be a novel effective anti-aging agent to progress the reconstruction of collagen and elastic fibres for the new approach of protective effect against collagen and elastin fibres disintegration on skin care cosmetics.



## References:

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