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A selected series of hydroxy-3-arylcoumarins as multitarget compounds for skin aging diseases

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pharmaceuticals MDPI

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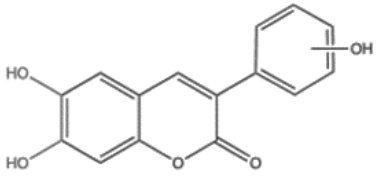
A selected series of hydroxy-3-arylcoumarins as multitarget compounds for skin aging diseases



HYDROXY-3-ARYLCOUMARINS

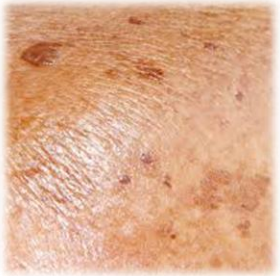
Elastase
Collagenase
Hyaluronidase

Degradation extracellular matrix proteins

UV

SKIN AGING

Tyrosinase



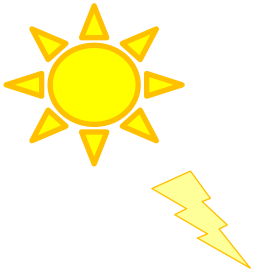
Hyperpigmented spots

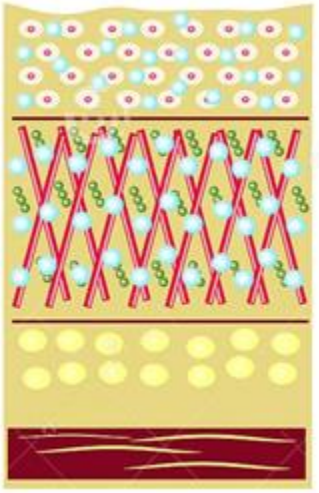
Abstract

Skin aging is a progressive biological process of the human body that depends, among several phenomena, on degradation of proteins of extracellular matrix as well as the appearance of hyperpigmented spots. In previous studies, we demonstrated that differently substituted 3-arylcoumarins efficiently inhibit skin aging-related enzymes, such as tyrosinase, elastase and collagenase. According to these considerations, we have modulated this scaffold to improve the inhibitory potency against tyrosinase, elastase and collagenase, extending the study to the inhibition another enzyme, hyaluronidase. Moreover, photo-protective effect of the compounds has been also evaluated by determining the Sun Protection Factor. Starting from 3-(3'-hydroxyphenyl)-6,7-dihydroxycoumarin and 3-(2'-hydroxyphenyl)-6,7-dihydroxycoumarin, that overall revealed to possess the best inhibitory effects against skin aging-related enzymes, we selected for this study new molecules including bromine atoms together with the previously studied hydroxyl groups. Some compounds present multitarget properties towards the selected enzymes, along with a good photo-protective effect. These data support our previous findings on 3-arylcoumarin as promising scaffolds for the design of skin anti-aging agents.

Keywords: Hydroxy-3-arylcoumarins; Tyrosinase; Elastase; Collagenase; Hyaluronidase.

Introduction

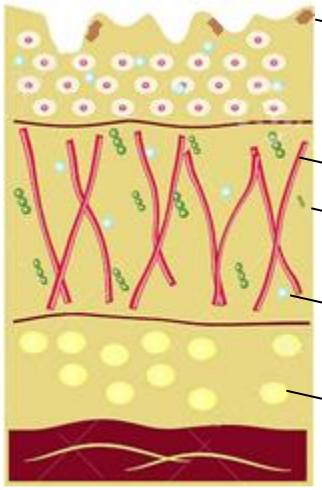




SKIN AGING

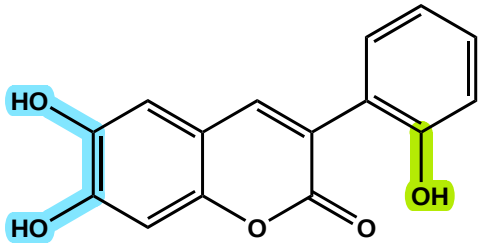
↑ Elastase
Collagenase
Hyaluronidase

↑ Tyrosinase

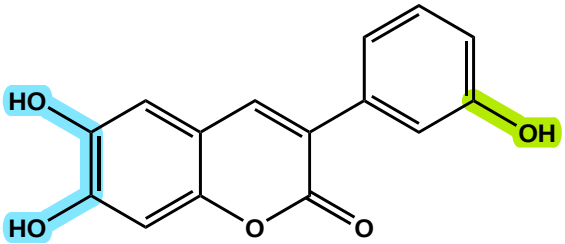


Introduction

1. Previously synthetized compounds



MJM555*

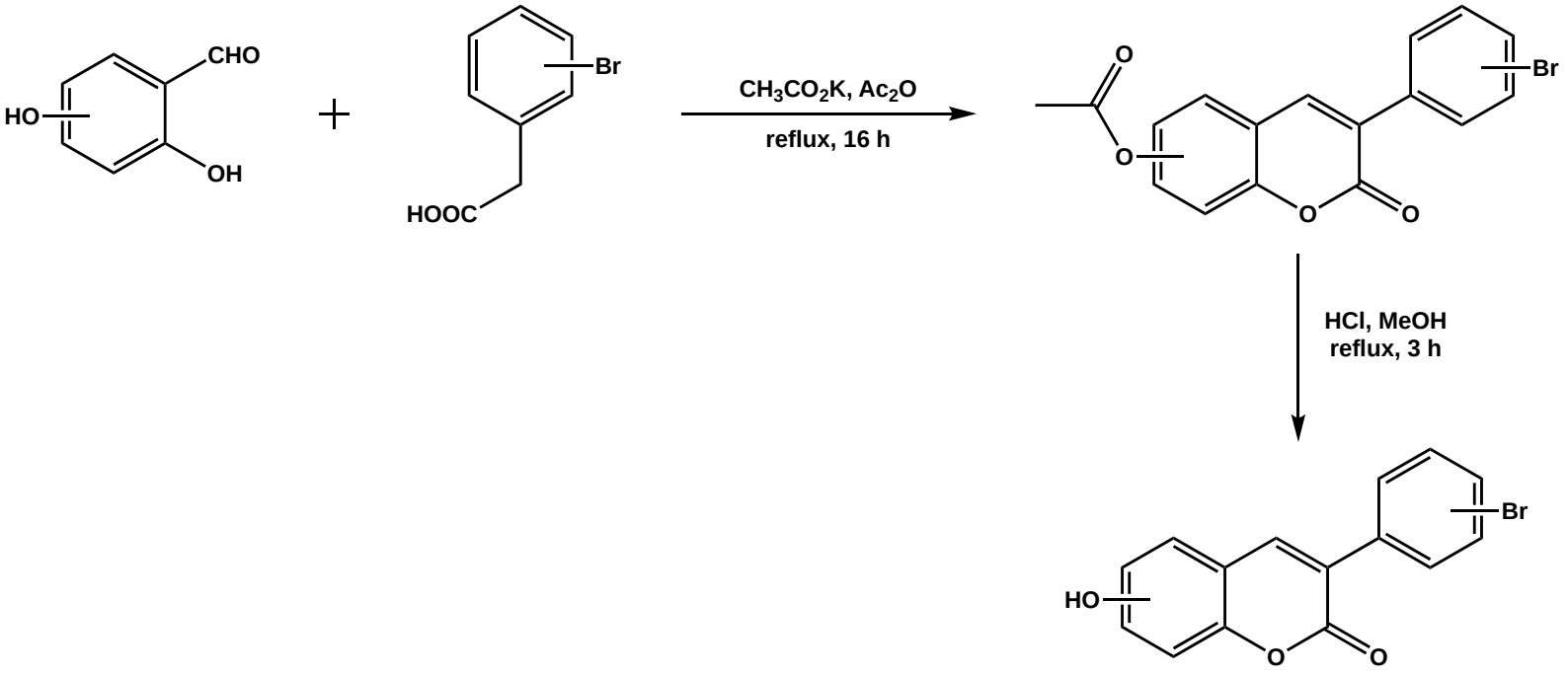


MJM556*

	Inhibition (%) 50 µM		Inhibition (%) 100 µM
Compounds	**Tyrosinase**	**Elastase**	**Collagenase**
MJM 555*	22.7	24.5	39.3
MJM 556*	8.6	29.6	35.7

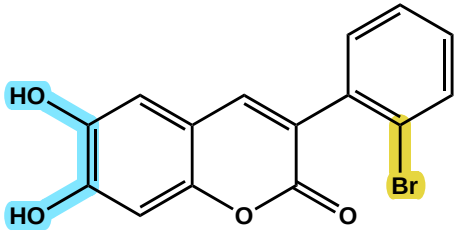
Introduction

2. Synthetic route to obtain the new compounds

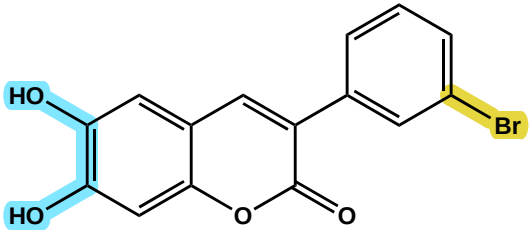


Introduction

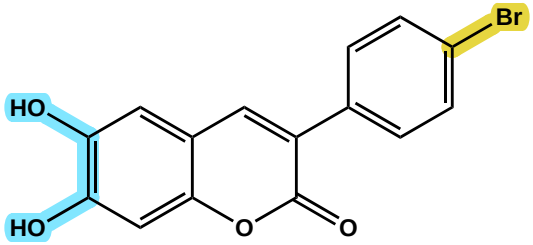
3. New synthetized compounds



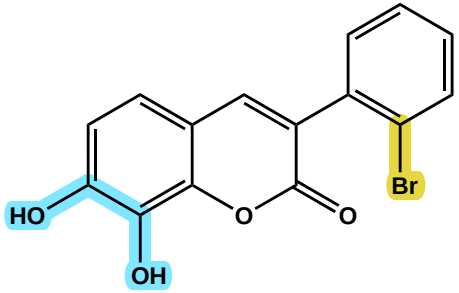
MJM558*



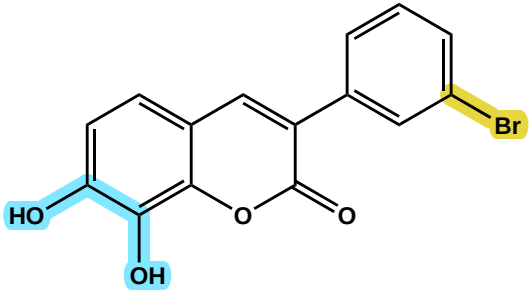
MJM559*



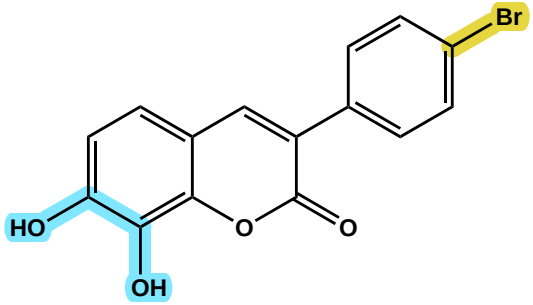
MJM566*



MJM560*



MJM561*



MJM562*

Results and discussion

- **Enzymatic Inhibition**

	Inhibition (%) 50 µM		Inhibition (%) 100 µM	Inhibition (%) 200 µM
Compounds	**Tyrosinase**	**Elastase**	**Collagenase**	**Hyaluronidase**
MJM555*	22.7[#]	24.5[#]	39.3[#]	14.2
MJM556*	8.6[#]	29.6[#]	35.7[#]	43.2
MJM558*	25.8	23.8	38.1	13.7
MJM559*	80.3	68.4	18.2	N.I.
MJM560*	15.7	N.I.	14.7	29.5
MJM561*	33.6	2.2	39.9	31.1
MJM562*	9.6	15.6	N.I.	18.1
MJM566*	58.3	30.5	N.I.	91.5

[#] = data previously reported
N.I. = No Inhibition

Results and discussion

- **Sun Protection Factor**

Compounds	SPF
MJM555*	5.64 ± 1.43
MJM556*	5.44 ± 0.64
MJM558*	8.08 ± 0.01
MJM559*	8.23 ± 0.64
MJM560*	4.27 ± 0.91
MJM561*	6.94 ± 2.57
MJM562*	5.88 ± 1.35
MJM566*	8.23 ± 0.14

Conclusions

- Compounds **MJM555***, **MJM556*** and **MJM558*** showed inhibitory activity towards all the four skin aging related enzymes, together with a good photoprotective effect.

- Compound **MJM559*** reveals to possess overall the higher inhibitory effect against tyrosinase and elastase, while the best inhibitory potential against hyaluronidase was showed by compound **MJM566***, both with a high SPF.

- These data support our previous findings on 3-arylcoumarin as promising scaffolds for the design of multitarget skin anti-aging agents.

Acknowledgments