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Use of grapevine cell cultures for the production of phytostilbenes of cosmetic interest

Utilisation de cultures cellulaires de vigne pour la production de phytostilbènes d'intérêt cosmétique

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ABSTRACT

Plant cell cultures constitute pesticide-free sources for obtaining plant secondary metabolites or plant extracts. Additionally, they do not contain any fungal contaminants, mycotoxins or heavy metals providing to the consumer potential health benefits and justifying the development of this technology at an industrial scale. Significant production levels of these secondary metabolites can be obtained through the use of elicitors, which activate plant defense mechanisms. Resveratrol, a well-known grapevine polyphenolic compound which possesses potent antioxidant and antiaging activities as well as a protective action on skin, is a good example of such plant secondary metabolites. Resveratrol and its oligomeric derivatives are used by several companies of cosmetic products but their extraction from vine stems and similar vegetal sources remains difficult. Therefore grapevine cell suspensions could represent interesting systems for the large-scale bioproduction of those compounds. Here we present an update of the methods used for the production of phytostilbenes by using grapevine cell cultures and the results obtained.

Mots clés:
Phytostilbènes
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RÉSUMÉ

Les cultures cellulaires végétales constituent une source de métabolites secondaires ou d'extraits végétaux dénués de pesticides. De plus, celles-ci ne contiennent aucun contaminant fongique, aucune mycotoxine ou métal lourd, ce qui confère au produit une valeur santé vis-á-vis des consommateurs et justifie le développement au niveau industriel de cette technologie. De grandes quantités de ces métabolites secondaires sont obtenues par l'utilisation d'éliciteurs qui sont capables d'activer les mécanismes de défense des plantes. Le resvératrol, un polyphénol de la vigne bien connu, qui possède des activités anti-oxydantes et anti-âge de même qu'il exerce une action de protection sur la peau, constitue un exemple de ce type de métabolite. Le resvératrol et ses dérivés oligomériques

Abbreviations: CDs, cyclodextrins; DW, dry weight; FW, fresh weight; JA, jasmonic acid; MeJA, methyljasmonate; SA, salicylic acid.

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sont déjà utilisés par plusieurs compagnies de produits cosmétiques, mais leur extraction à partir de sarments de vigne ou de sources végétales similaires demeure difficile. Les suspensions cellulaires de vigne représentent donc des systèmes intéressants pour la production en grandes quantités de ces composés. Nous présentons ici une mise au point sur leurs méthodes de bioproduction en cultures cellulaires et les résultats obtenus.

1. Introduction

Polyphenol *trans*-resveratrol (*trans*-3,5,4'-trihydroxystilbene) is a famous member of the stilbene family as this compound has been associated with the "French paradox" (Fig. 1). Its daily consumption, for example, in the form of red wine [1], has been linked to beneficial effects in humans [2] and protection against coronary heart diseases [3]. First isolated from the white hellebore (*Veratrum grandiflorum O.* Loes) [4], it was then also found in Japanese knotweed (*Polygonum cuspidatum* syn. *Fallopia japonica*) [5], the current source for its industrial extraction in China. In grapevine leaves and berries, *trans*-resveratrol is a phytoalexin produced in response to stresses, such as wounding or pathogen attack [6] showing an antifungal activity against plant pathogens [7–11] or human pathogens [12]. In grapevine stem (wood) resveratrol is produced constitutively and acts as a phytoanticipin. In humans, resveratrol might play a role in preventing cardiovascular diseases [13]; it might also provide some protection against certain types of cancer [14], diabetes [15] and retard some neurodegenerative diseases [16]. In metazoans and mice, resveratrol has been demonstrated to extend lifespan by acting as a mimic-agent for the caloric restriction-longevity effect through sirtuin protein activation [17,18]. Nowadays, the main market for resveratrol is in the nutraceuticals sector using the *Polygonum* root as a source but some American companies have focused on grapevine as the raw material (Longevinex®). In the cosmetics field, the grapevine seems to be the most suitable raw material for resveratrol and its derivatives for products such as face creams [19,20].

The role of resveratrol in skin protection has to be linked first to its well known antioxidant properties. For example, in a study evaluating the peroxydal scavenging activities of various wine polyphenolic monomers, resveratrol was found to be the strongest compound over catechin, epicatechin/gallocatechin and gallic acid/ellagic acid [21]. In the same way, a formulation containing 1% resveratrol (FAMAR, Athens, Greece) developed for Calidora Skin Clinics (Seattle, WA) has shown a 17-fold increase in antioxidant potency against a formulation containing 1% of the coenzyme Q analog idebenone using the ORAC test (Oxygen Radical Absorbance Capacity, Brunswick Laboratories, Norton, MA), the latter compound being recognized as the strongest topical antioxidant [22]. The resveratrol skin care formulation indeed yielded 4845 μmoles vitamin E equivalents/g against 279 for the 1% idebenone-containing formulation [23]. Another aspect of interest is the potential role of resveratrol and derivatives as whitening agents in cosmetology. Tyrosinase (monophenol, dihydroxyphenylalanine: oxygen oxidoreductase EC 1.14.18.1) is a

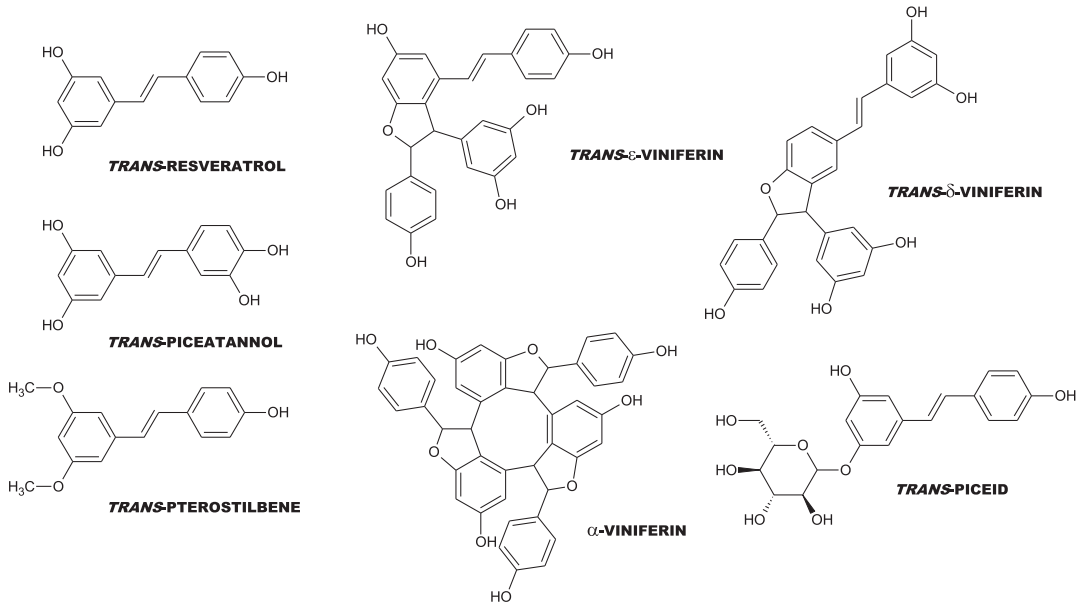

Fig. 1. Chemical structures of some hydroxystilbene monomers and dimers.