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Development of a natural ingredient – Natural preservative:  
A case study*Développement d'un ingrédient naturel: Étude de cas d'un conservateur naturel*Audrey Kerdudo<sup>a, b</sup>, Pauline Burger<sup>a</sup>, Florence Merck<sup>a</sup>, Alexandre Dingas<sup>b</sup>,  
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## ABSTRACT

Lately, the cosmetic and personal care market has been more and more driven toward natural ingredients by the rising consumers' awareness about personal health and safety and their will for safer cosmetics free of harmful chemicals. Preservatives are no exception to the rule: evidence or suspicion of the toxicity of certain synthetic preservatives that have been around for decades pushed the cosmetic industry forward to seek for natural alternatives, as the selection of natural preservatives already available is quite limited. Sourcing active metabolites and developing new natural ingredients are long-term procedures that are thoroughly described in the present paper, via the example of the design of a natural preservative based on the *Santolina chamaecyparissus* extract, and of the assessments of its preservative effectiveness.

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## R É S U M É

Récemment, sous la pression grandissante de consommateurs toujours plus avertis en matière de santé publique, le marché de la cosmétique s'est tourné vers les ingrédients naturels afin de formuler des produits cosmétiques plus sûrs et dénués autant que faire se peut de produits chimiques dangereux. Les conservateurs ne constituent pas une exception : les suspicions et preuves de toxicité de certains conservateurs de synthèse, pourtant utilisés depuis des décennies, ont impulsé la recherche en matière de solutions alternatives naturelles, étant donné qu'à l'heure actuelle le choix en matière de conservateurs naturels est encore restreint. Le *sourcing* de métabolites secondaires et le développement de nouveaux ingrédients naturels, procédures de longue haleine, sont décrits dans cet article, à travers l'exemple du développement d'un conservateur naturel à base d'extrait de *Santolina chamaecyparissus* et de l'évaluation de ses propriétés conservatrices.

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## 1. Introduction

The worldwide cosmetic industry has largely developed over the past decade (worth expected to reach \$390 billion by 2020; [1]) and its solid growth continues to be driven essentially by consumers expecting increasingly innovative products, as well as efficacy and quality. However, rising awareness about personal health and safety also led the consumers to look forward to safer cosmetics free of harmful chemicals. Hence, the dramatically increasing global trade in natural ingredients sourced from vegetable, mineral or marine renewable sources has perfectly illustrated this important trend in the last years. The predominance of such natural ingredients is largely due to the various roles they can play in a single cosmetic formula, acting as active ingredients (e.g., moisturizers), excipients (e.g., surfactants), additives (e.g., preservatives), etc., the last ones being particularly sought for by cosmetic manufacturers.

Microbial growth could occur in cosmetics and personal care products under usual manufacturing and usage conditions and numerous sources of contamination have been identified: the raw materials, the packaging, or even the manufacturing processes and environments that are often not sufficiently sterile. These products can also be exposed to temperature variations, and be notably subject to temperatures higher than recommended in shops and consumers' bathrooms, hence increasing the micro-organism growth rate. Furthermore, once the cosmetic or personal care product is opened, and until it is discarded, it is highly susceptible to further contamination due to consumer use (constant dipping of non-sterile fingers in the product, contact with non-sterile bodies, etc.). Micro-organisms can hence easily multiply and cause unpleasant discolouration and odour, and can degrade active compounds in products, leading to the instability of finished products [2,3]. Cosmetics and personal care products are hence expected to resist microbial attack within their intended period of use [4]: preservatives are then necessary to prevent product spoilage and subsequently consumers' infections caused by harmful micro-organisms. Strict rules govern the inclusion of preservatives in cosmetics. Throughout Europe, manufacturers must carefully choose among preservatives listed in Annex V of Regulation (EC) [4] that have previously been subjected to scientific tests and approval procedures: every cosmetic formulation requires a tailor-made preservative system to meet its specific needs (selection of the appropriate nature and dosage of a specific preservative) [5].

Synthetic preservatives employed over decades such as *p*-hydroxybenzoic acid, phenoxyethanol and imidazolidinyl urea [3], display a whole lot of benefits including notably their more than affordable price, their broad-spectrum of activity against bacteria and fungi, their compatibility with other ingredients, and the fact that they generally do not interfere with fragrance, colour, or other aspects of a given formulation. However, although common synthetic preservatives do extend the lifespan of the products and help to keep them free from micro-organisms, many of them have developed negative

reputations in consumers' minds and their use has become more and more controversial over the last years. In fact, often petroleum-based, they can be unhealthy and can notably promote irritations or infections, particularly on damaged skin, or the sensitive areas around the eyes [6]. Some of them can even cause higher health issues: 4-hydroxybenzoic acid esters, better known as parabens have been the most widely used preservatives (entering the composition of about 80% of the worldwide cosmetics; [7]), but have recently been reported to mimic oestrogen, to increase female breast cancer incidence and to influence the development of malignant melanoma [8]. Following the controversies about parabens and phenoxyethanol, cosmetic formulators are under increased pressure to turn more and more to innovative natural ingredients [7], because they are not only healthier alternatives for consumers but they also provide a wonderful marketing angle. In fact, the discovery and usage of a natural ingredient with preservative properties offers cosmetic industries the chance to communicate about the "preservative free" aspect of their products, as these new natural ingredients do not fall under the legislation and are hence not listed among preservatives in Annex V of Regulation (EC) [4]. Furthermore, if such a natural ingredient, besides its preservative action, also displays another interesting property, e.g., anti-oxidizing effect, the marketing communication opportunities will become even larger. Finally, rising consumer demand for products formulated with natural raw materials also offers cosmetic companies a chance to raise the awareness of consumers to biodiversity that becomes a strategic issue as a rich source for innovative molecules. Sourcing new natural ingredients engage cosmetic industries in a 'green economy' policy presided over by the respect of the principles of the Nagoya Protocol introduced on 29 October 2010, and issued from a number of implements of the original Convention on Biological Diversity (CBD) ratified in 1992 by 168 States at the United Nations' Earth Summit held in Rio de Janeiro [9]. The CBD constituted the first international document to recognize the urgent need to protect biodiversity, the sustainable use of its resources, and the equal and rightful sharing of the benefits it represents. Application of high throughput screening technologies to natural product samples accelerates the discovery, development and use of natural ingredients but such a screening is still a long-term undertaking as only five in every 100 genetic resources identified as being potentially of interest will ever end up in cosmetic and personal care formulae as they also have to pass all the efficacy, quality and safety tests right throughout the development chain [10].

Regions presenting high biodiversity and a high percentage of endemic flora and fauna that are especially endangered are recognized as biodiversity hotspots [11,12] and constitute protection priorities. With the generalized awareness of this richness threatened with extinction it appeared worth preserving this biodiversity and valuing plant species in the form of new ingredients intended notably for cosmetic and pharmaceutical industries. The Mediterranean region was identified as one of these biodiversity hotspots [12] due to its remarkable flora and specially its high rate of endemic species:

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