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Review

Market Transformation in Dandruff Control: Recent Developments on Anti-Dandruff Active Ingredients

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Abstract

After the European Union's ban of zinc pyrithione from cosmetic use, piroctone olamine, climbazole, and salicylic acid have become the most common anti-dandruff active ingredients used in cosmetics today. Other conventional chemistries and less frequently used active ingredients, like hexamidine diisethionate and selenium sulfide, have also seen a recent upward trend. Entirely new technologies, like propanediol caprylate and propanediol undecylenate, are only in their initial stages but are ready to change the industry. The aim of the following study is to holistically characterize these compounds, regarding their chemical data, mode of action, and study results, where available, to shed light on the pros and cons and to take a detailed look at environmental considerations, market situation and regulatory aspects. In addition, many commercially available anti-dandruff consumer products combine multiple active ingredients to address the multifaceted nature of the condition, often targeting both fungal activity and scalp inflammation.

Keywords: dandruff; US FDA monograph for dandruff control; EU cosmetics regulation; China; zinc pyrithione replacement; piroctone olamine; climbazole; salicylic acid; propanediol caprylate/undecylenate; decylene glycol

1. Introduction

Dandruff, characterized by itchy, flaky skin with white or yellowish scales, is a common scalp condition affecting around 50% of the global population [1]. Dandruff and seborrheic dermatitis (SD) are considered a continuous spectrum of the same skin disorder, differing only in locality and severity. Although their exact cause is not fully understood, it is expected to result from various intrinsic and environmental factors, including individual susceptibility, sebaceous secretion, immune response, and the activity of microorganisms [1–3]. Lipophilic *Malassezia* yeasts have long been regarded as a key causative factor. However, recent advancements have enabled a more comprehensive evaluation of the scalp microbiome, including bacterial balances, with indications that the overall relative composition, as well as the interactions between individual components, may be of importance in dandruff development [4,5].

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However, as summarized and discussed in [6], current studies on the microbiome of healthy and dandruff-affected scalps are limited in their conclusions, especially by small sample sizes, short intervention periods and methodological heterogeneity.

Among the multiple chemical entities that are effective in counter-acting SD and dandruff, such as azoles (i.e., ketoconazole, climbazole), hydroxypyridones (i.e., piroctone olamine (PO), ciclopirox olamine), allylamines (i.e., terbinafin), selenium sulfide, zinc pyrithione (ZPT) and propanediol caprylate (PMC) or propanediol undecylenate (PMU), the common mechanism of action is their anti-fungal activity [6,7]. However, they also have positive effects on the dysbiosis of the scalp microbiome by influencing the bacterial microbiota [5,6].

As ZPT was banned from cosmetics in the EU [8], this article summarizes the characteristics of the most common anti-dandruff active ingredients currently used in cosmetics globally, including piroctone olamine, climbazole and salicylic acid; furthermore, this article examines less frequently used active ingredients, like hexamidine diisethionate, selenium sulfide, the new ester technologies, PMC and PMU, and the multifunctional decylene glycol. In order to also reflect the current situation in more strictly regulated markets like North America, we are covering the entire positive list of active ingredients from the US FDA monograph for dandruff control, except for ZPT (Figure 1), thereby also adding sulfur and coal tar to the list of active ingredients. The overall examination includes data on chemistry and pharmacology, mode of action, efficacy and influence on the microbiome, ecotoxicology, market aspects and regulations. As active ingredients are often combined in commercially available anti-dandruff products, study results of these combinations are included in this overview.

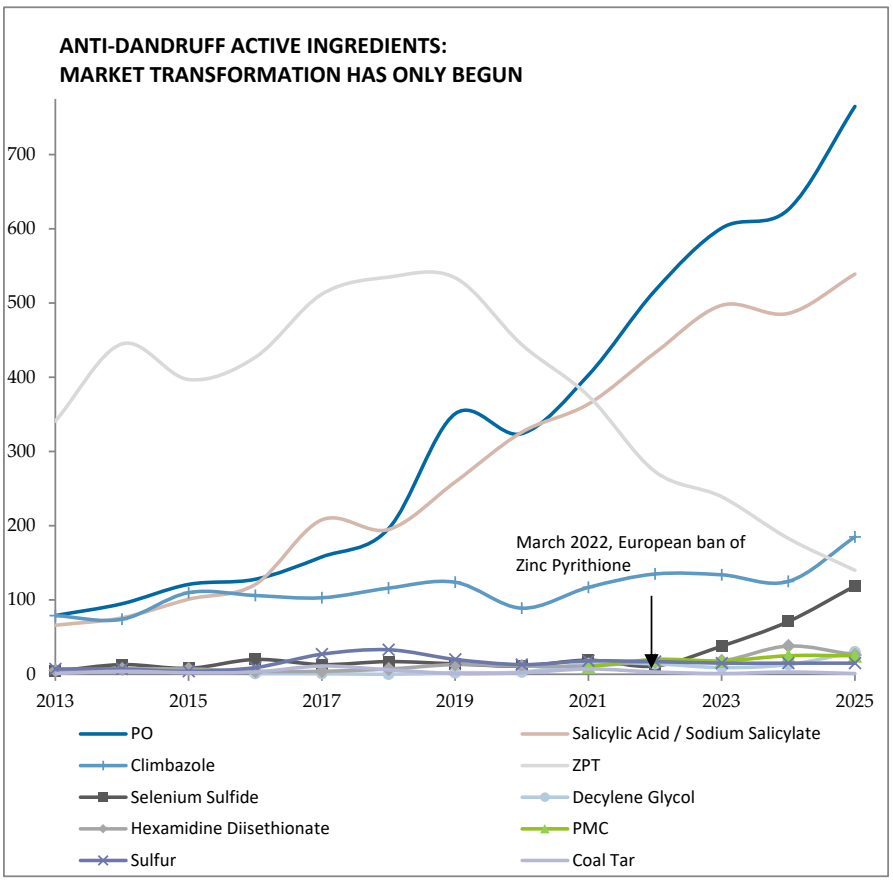


Figure 1. Number of new variants with anti-dandruff claims identified in the consumer market globally, by calendar year and including the respective anti-dandruff active ingredient, as per Mintel GNPD data, with 2025 numbers for: PO (765), salicylic acid/sodium salicylate (539), climbazole (185), ZPT (140), selenium sulfide (119), decylene glycol (30), hexamidine diisethionate (26), PMC (25), sulfur (15), and coal tar (1) [9].

2. Anti-Dandruff Active Ingredients

This section provides a comprehensive overview of the anti-dandruff active ingredients currently utilized in cosmetic products globally. The databases PubMed and SciFinder were searched for data in July 2025. Search terms included, but were not limited to, "dandruff", "piroctone olamine", "climbazole", "salicylic acid", "hexamidine diisethionate", "selenium sulfide", "propanediol caprylate", "propanediol undecylenate", "decylene glycol", "coal tar", "microbiome", "scalp", "mechanism", and "ecotoxicology". Table 1 provides a concise overview of their key environmental and ecotoxicological properties.

According to updated regulatory frameworks, the following newer ratings have been assessed. *Persistent, bioaccumulative, and toxic/very persistent, and very bioaccumulative* (PBT/vPvB) represents a classification scheme under REACH [10] and other frameworks aiming to identify substances that are not biodegradable (*persistent*), thus having the potential to accumulate in living organisms through the food chain (*bioaccumulative*), and causing adverse effects to organisms (*toxic*).

Persistent, mobile, and toxic/very persistent, and very mobile (PMT/vPvM) furthermore represents a new classification scheme under the CLP regulation [11,12], aiming to identify substances that are not biodegradable (*persistent*); have a high potential to move through soil, thus contaminating groundwater resources; and cause adverse effects (*toxic*). The newly implemented criterion *mobile* is assessed via the log Koc (*organic carbon–water partition coefficient*). If the log Koc of a substance is above 2, it is not considered *very mobile* (vM), and above 3, it would not be considered *mobile* (M), therefore posing a low risk.

Table 1. Environmental fate and aquatic toxicity data of anti-dandruff active ingredients.

INCI **CAS No.**	**Piroctone Olamine** [13] **68890-66-44**	**Climbazole** [14] **38083-17-9**	**Salicylic Acid** [15]/ **Sodium Salicylate** [16] **69-72-7, 54-21-7**	**Hexamidine Diisethionate** [17] **659-40-5**	**Selenium Sulfide** [18] **7488-56-4**	**Propanediol Caprylate** [19] **102731-54-4**	**Propanediol Undecylenate** [20] **176504-44-2**	**Decylene Glycol** [21] **1119-86-4**	**Coal Tar** [22] **80007-45-2**
Biodegradation	not biodegradable	not biodegradable	readily biodegradable	not biodegradable	n.a.	readily biodegradable	readily biodegradable	readily biodegradable	n.d.
Bioaccumulation (based on log Kow)	3.2	3.83	2.64	4.47	n.a.	3.33	4.78	1.99	n.d.
Mobility (based on log Koc)	3–5.4	3.74	1.54	5.07 *	n.a.	1.54 *	2.53 *	1.2 *	n.d.
Toxicity, fish, acute (LC50), chronic (NOEC/EC10)	5.1 mg/L 0.67 mg/L *	1.9 mg/L 0.014 mg/L	1380 mg/L 20.2 mg/L	9.76 mg/L n.d	24 mg/L n.d.	4.52 mg/L n.d.	7.99 mg/L n.d.	14.1 mg/L n.d	7.33 mg/L n.d.
Toxicity, *Daphnia*, acute (EC50), chronic (NOEC)	1.8 mg/L 0.13 mg/L	10.9 mg/L 0.2 mg/L	870 mg/L 10 mg/L	0.076 mg/L n.d	>100 mg/L n.d.	10 mg/L n.d.	2.5 mg/L n.d.	25.5 mg/L n.d	4.44 mg/L n.d.
Toxicity, algae, acute (EC50), chronic (NOEC/EC10)	10.8 mg/L 6.3 mg/L	0.024 mg/L 0.008 mg/L	>100 mg/L 60–120 mg/L	0.059 mg/L n.d.	>100 mg/L ≥100 mg/L	3.7 mg/L 0.12 mg/L	5.9 mg/L * n.d.	41.3 mg/L 22.7 mg/L	n.d. n.d.
PBT/vPvB and PMT/vPvM potential	none	none	none	none	n.a.	none	none	none	n.a.
GHS hazard classification	H401/H412	H400/H410	none	H400/H410	H402 (H400/H410) **	H401/H411	H401/H411	H402	n.a.

All values are experimental results, except those marked * = QSAR prediction; ** = harmonized classification according to CLP regulation [11]. n.a. = Not applicable; n.d. = no data; LC50 = median lethal concentration; NOEC = no observed effect concentration; EC10 = 10% effective concentration.

2.1. Piroctone Olamine

2.1.1. Chemistry/Pharmacology

PO (CAS RN: 68890-66-4) is the ethanolamine salt of a 2-pyridone derivative, a synthetic hydroxypyridone [23–25]. It has the chemical name 1-hydroxy-4-methyl-6-(2,4,4-trimethylpentyl)-2(1 H)-pyridone, ethanolamine salt. PO is a solid with a melting point of 130–136 °C, MW 298.43 g/mol. It is nearly insoluble in water, mineral oil, cosmetic esters, vegetable oils and silicones, has limited solubility in glycerin, but dissolves well in ethanol, glycols and surfactants. The use concentration for anti-dandruff applications can be chosen between 0.1 and 1.0%, depending on the desired finished product. Local adverse effects like irritation, swelling, pain, and allergic contact dermatitis are rare.

2.1.2. Mode of Action

Hydroxypyridones like PO, or ciclopirox olamine on the pharmaceutical side, differ in their structure and mechanism of action from all other known anti-fungal substances [26–28]. The activity profile includes all clinically relevant dermatophytes, yeasts, including *Malassezia*, and molds. While many anti-fungals interfere with fungal ergosterol metabolism, primarily acting on the cell membrane, hydroxypyridones act on fungal cells in a variety of ways:

A central mechanism of action is the binding (chelation) of polyvalent metal cations such as iron (Fe^{2+}, Fe^{3+}) and aluminum (Al^{3+}), thus impairing the function of metal-dependent enzymes (cytochromes, catalases, peroxidases). This has repercussions on a variety of cellular processes (Table 2).

Table 2. Postulated anti-fungal targets of ciclopirox olamine (adapted from [27]).

• High-affinity chelation of polyvalent metal cations, particularly intracellular iron (Fe^{2+}, Fe^{3+}), thereby
o Inhibition of metal-dependent enzymes (cytochromes, catalases, peroxidases), thus a. Disruption of cellular processes such as mitochondrial electron transport, energy production, and uptake of nutrients and their precursors through the cell membrane b. Inhibition of RNA and thus also protein synthesis c. Alteration of membrane permeability, which leads to intracellular transport disturbances, especially of precursors d. Disruption of DNA repair mechanisms and cell division, particularly through impaired formation of the mitotic spindle e. Reduced degradation of reactive oxygen species by inhibiting the fungal catalase f. At higher concentrations, destruction of the cell membrane with release of potassium ions and other intracellular material

2.1.3. Efficacy and Influence on Microbiome

Due to this broad mode of action PO has fungistatic, fungicidal, and sporicidal effects, meaning that, unlike many other anti-fungals, it also targets dormant, non-metabolically active fungal elements. Furthermore, the development of resistance has not yet been described. In addition to its fungicidal properties, PO also has bactericidal effects against Gram-positive and Gram-negative bacteria. Recently Hu et al. showed that the scalp microbiome after 3 weeks of treatment with an anti-dandruff shampoo containing 0.5% PO reduced the relative abundance of *Malassezia* species and *Staphylococcus capitis* and increased the relative abundance of *Cutibacterium acnes*. This change was consistent with an improvement of clinical signs [29].

Due to its diverse targets and potential synergistic effects with other anti-fungal classes, PO is also ideal for use in combination treatment of dandruff.

2.1.4. Ecotoxicology

Environmental Fate and Distribution

Different biodegradability studies show that PO is not biodegradable [13,30]. Since PO is a weak acid, it can be ionized depending on pH. The log Kow values (Table 1) measured at different environmentally relevant pH values (pH 4, pH 7 and pH 9) are all below the European CLP regulation's cut-off values of 4 (criterion for bioconcentration in aquatic organisms) and 4.5 (criterion for bioaccumulation) [11,12], therefore the bioaccumulation potential of PO is low. Furthermore, PO is considered immobile in soil based on various measured log Koc values (Table 1) which are all above the CLP regulation's mobility criteria [12].

Aquatic Toxicity

PO is acutely toxic to fish, Daphnia and algae. The determined effect concentrations of short-term toxicity studies are all in the range between 1 and 10 mg/L (Table 1). Experimental and predicted long-term toxicity data show harmful effects on *Daphnia* (NOEC = 0.13 mg/L) and fish (NOEC = 0.67 mg/L) and no toxic effects on algae (EC10 = 6.3 mg/L).

Taking into account this data, PO is considered to be classified in acute aquatic toxicity cat. 2 (H401) and in chronic aquatic toxicity cat. 3 (H412) according to the GHS classification scheme [31]. Furthermore, the data set indicates that PO is neither a potential PBT/vPvB nor a potential PMT/vPvM substance according to the CLP regulation's recent amendment (EU) 2023/707 implementing new hazard classes as part of the EU green deal [12].

2.1.5. Market Aspects and Regulations

PO was first patented as an anti-dandruff active by Hoechst AG, Frankfurt, Germany (now Clariant) in 1972 [32] and marketed under the brand name Octopirox. In a ZPT-dominated cosmetic market, PO was second choice alongside climbazole until 2015. In the last ten years the consumer market for dandruff control has undergone a fundamental change, with PO being the number one choice for most manufacturers, replacing ZPT in the EU market. Today PO is by far the most frequently used anti-dandruff active as can be seen in Figure 1. Until this change PO had been an expensive option, but with global volumes increasing dramatically, its market price has dropped significantly. PO is not approved as an anti-dandruff active by the US FDA monograph [33]. In the EU market, anti-dandruff shampoos are allowed a use concentration of up to 1%, while for leave-on cosmetics a maximum dose of 0.5% applies. Like most other conventional actives for dandruff control, PO is regulated by EU Cosmetics Regulation 1223/2009, Annex V (*List of Preservatives Allowed in Cosmetic Products*) entry 35 [34]. Similar rules apply in the Chinese market, where 1-hydroxy-4-methyl-6(2,4,4-trimethylpentyl)2-pyridon and its monoethanolamine salt are limited to 1.0% for rinse-off products and 0.5% for other products as per the National Medical Products Administration's (NMPA) Safety and Technical Standards for Cosmetics (STSC) [35]. From a chemical regulation perspective, the ingredient is EU REACH [10] registered with 28 registrations in place [14].

2.2. Climbazole

2.2.1. Chemistry/Pharmacology

Climbazole (CAS 38083-17-9, IUPAC name 1-(4-chlorophenoxy)-1-(1H-imidazol-1-yl)-3,3-dimethylbutan-2-one) is an imidazole anti-fungal, a heterocyclic organic compound used in cosmetics, particularly in anti-dandruff shampoos. It is a white to off-white crystalline powder and is only slightly soluble in water but highly soluble in cosmetic solvents and fragrance oils. It is light- and heat-stable and easy to store. A use concentration

of up to 0.5% climbazole in both leave-on and rinse-off formulations has been most common from global perspective, though a use concentration in rinse-off shampoos up to 2% is possible case by case [36].

2.2.2. Mode of Action

Climbazole inhibits the growth of fungi such as *Malassezia*, which are important for dandruff formation. All azole anti-fungals exert their fungistatic effect by inhibiting ergosterol biosynthesis, and lanosterol 14α-demethylase is inhibited [37,38]. The resulting deposition of false sterols disrupts normal membrane function, particularly impairing the function of membrane-bound enzymes.

2.2.3. Efficacy and Influence on Microbiome

The inhibition of ergosterol biosynthesis also means in principle that azoles are only fully effective against proliferating fungi but not against fungal spores or mycelium in the dormant phase which do not synthesize new ergosterol. Azole-resistant *Malassezia* spp. may be of importance [39].

Azoles also exhibit anti-bacterial properties. For example, miconazole is active against Gram-positive bacteria, particularly *Streptococcus* spp. and *Staphylococcus* (S.), and notably also against methicillin-resistant (MRSA) and fusidic-acid-resistant (FRSA) *S. aureus* strains [40]. Its activity against bacteria may be due to the presence of lanosterol 14-demethylase homologues in *Staphylococci*. Recently, anti-bacterial activity has also been correlated with the inhibition of bacterial flavohemoglobins [41]. These play an important role in bacterial resistance to reactive nitrogen species. As a common characteristic of most anti-dandruff actives in the market, climbazole shows effects against *S. aureus* which is reflected in a MIC of 250 ppm [6].

2.2.4. Ecotoxicology

Environmental Fate and Distribution

Climbazole was not biodegradable in different biodegradability screening tests (OECD 301, 302) [42]. However, an aerobic sewage treatment simulation test (OECD 303 A) showed some degradation of climbazole and indicates that biodegradation is an important route of elimination for this substance in sewage treatment plants [43]. This might be the reason why measured concentrations of climbazole found in the environment (surface water of rivers and lakes and in ditches) are very low (<0.6 µg/L) and, therefore, do not indicate a risk for aquatic organisms [44–46]. Furthermore, the measured log Koc value of 3.74 (Table 1) indicates low mobility of climbazole in soil [11,12]. Additionally, the bioaccumulation potential of climbazole can be considered low, since the experimentally determined log Kow of 3.83 (25 °C and pH 10) is below the cut-off values of 4 (criterion for bioconcentration in aquatic organisms) and 4.5 (criterion for bioaccumulation in aquatic organisms) [11,12]. Furthermore, in vivo toxicokinetic studies with vertebrates show that climbazole will be rapidly metabolized in air-breathing organisms (within hours) [47–49].

Aquatic Toxicity

Several short-term and long-term toxicity data for various aquatic species on different trophic levels are available for climbazole (Table 1). The acute results show that fish and *Daphni*a are clearly less sensitive compared to aquatic plants. The tests with aquatic plants show high acute toxicity with EC50 values in the range of 0.0239 mg/L for duck weed to 1.19 mg/L for algae species [50]. The results for long-term toxicity indicate that *Daphnia* are less sensitive than fish and aquatic plants (EC10 = 0.008 mg/L for duck weed as the most sensitive species [50]).

Taking into account all available data, climbazole is considered very toxic for aquatic organisms, leading to an acute aquatic toxicity cat. 1 (H400) and a chronic aquatic toxicity cat. 1 (H410) classification according to the GHS classification scheme [31]. Climbazole is neither a potential PBT/vPvB nor a PMT/vPvM substance [11,12].

2.2.5. Market Aspects and Regulations

Similar to PO, climbazole's history also goes back to the 1970s with a first trade name Baypival originating from Bayer AG, Leverkusen, Germany and the related patent DE2430039 titled "*Azole antimycotics and their use in treating skin conditions caused by Pityrosporum ovale or Azole Antimycotics in Cosmetics*" was filed in June 1974 [51]. Under Bayer's former subsidiary Haarmann & Reimer, Holzminden, Germany (today Symrise) Baypival was marketed as Crinipan AD. The number of final formulations launched in the global cosmetic market using climbazole has been relatively stable over the last 20 years (see Figure 1). Climbazole keeps its market share from a global perspective, especially due to its cost effectiveness. While its use in the EU has been declining lately, increased growth resulting from ZPT replacement can be seen, especially in emerging markets. The fact that climbazole has not been growing as strongly as PO can be explained with a general tendency of today's cosmetic market to move away from azole technologies, for example, due to (eco)toxicological read-across within this group of chemicals and resulting concerns not primarily derived from climbazole itself.

Climbazole is not approved as an anti-dandruff active by the US FDA monograph [33]. In the EU market, anti-dandruff shampoos are allowed up to 2% as per cosmetics regulation Annex III (*List of substances which cosmetic products must not contain except subject to the restrictions laid down*) entry 310. For other uses a dosage of up to 0.2 to 0.5% depending on the application applies as per Annex V entry 32 (*climbazole, maximum concentration in ready for use preparation: Rinse-off shampoo 0.5%; hair lotions/face creams/foot products 0.2%*) [34]. For many years a generic maximum use level of 0.5% climbazole as a preservative has been established in the EU. Only in 2019 were the individual levels described above implemented in regulations specifically naming the *anti-dandruff* function [36]. As a result, a 2% use level is not expected to be common practice in the market, but a use level up to 0.5% is expected to still be representative for most products sold today. The former 0.5% EU maximum dose also still applies in the Chinese market as per NMPA's STSC today [35]. Lately, China's National Institute for Food and Drug Control (NIFDC) announced upcoming further restrictions on climbazole's use levels in a public consultation in September 2025, and on 12 January 2026 NMPA officially released its final revision. The new limits effective 1 January 2028 are as follows: Rinse-off hair products up to 0.5%; and up to 0.2% for leave-on hair products, face products (including neck), eye products and lip products.

From a chemical regulation perspective, climbazole is EU REACH registered by Symrise as the sole registrant [14].

2.3. Salicylic Acid/Sodium Salicylate

2.3.1. Chemistry/Pharmacology

Salicylic acid (CAS 69-72-7) or 2-hydroxybenzoic acid is an organic compound with the formula $C_7H_6O_3$. It is a colorless to white, odorless powder, with limited solubility in water. It is soluble in ethanol, glycols (e.g., propylene glycol, butylene glycol) and oils [52,53]. Initially identified and derived from willow trees (Salix alba, hence the name), salicylic acid has a long history of safe use in medicine and skin care treatments [54]. It is even listed on the World Health Organization's List of Essential Medicines as one of the most important medicinal ingredients in the world [55].

2.3.2. Mode of Action

When used in shampoo, salicylic acid is applied particularly for its keratolytic effect, supporting the removal of excessive dead skin flakes (dandruff) from the scalp. The cohesion between stratum corneum cells is diminished and disintegrated, thus easing the shedding of the dead skin cells at the superficial skin layer. Increased proliferation leads to impairment of the keratinization process, with the resulting detachment of great cell complexes [7,54,56]. Salicylic acid also has anti-microbial effects [7,54]. Normally a 1.5–3% concentration of salicylic acid is used in shampoos for keratolytic effects [57].

2.3.3. Efficacy and Influence on Microbiome

Even in quite low concentrations, salicylic acid is known to exhibit bactericidal activity, which is pH-dependent. This efficacy even expands towards the reduction of bacterial biofilms, both under development (e.g., *Pseudomonas aeruginosa* [58]) or fully developed (*Escherichia coli* [59]). Often labeled as a natural alternative to "harsh" anti-microbials the bactericidal efficacy of salicylic acid is probably due to enzyme inhibition. Side effects may be burning or stinging at the application site [7].

2.3.4. Ecotoxicology

Environmental Fate and Distribution

Salicylic acid is readily biodegradable based on a variety of biodegradability studies [15,16]. Several experimentally determined log Kow values can be taken into account for the bioaccumulation assessment (Table 1). The bioaccumulation potential of salicylic acid can be considered low, since these log Kow values are all below the cut-off value for bioconcentration and bioaccumulation [11,12]. However, salicylic acid shows a high mobility in soil indicated by the experimentally determined log Koc value and therefore fulfills the mobility criteria according to the CLP regulation [11,12].

Aquatic Toxicity

Several experimental short-term and long-term toxicity data for various aquatic species on different trophic levels are available for salicylic acid [15,16]. The most reliable results indicate neither short-term nor long-term toxic effects on fish, *Daphnia* and algae/aquatic plants (acute LC50/EC50 values > 100 mg/L; chronic NOEC/EC10 values > 1 mg/L) (Table 1).

Based on this data set, salicylic acid is considered not harmful for aquatic organisms and the substance neither meets the criteria for PBT/vPvB nor for PMT/vPvM [11,12].

2.3.5. Market Aspects and Regulations

Salicylic acid has been steadily growing over the last 10 years in terms of product variants launched to market for dandruff control (see Figure 1) using either the acid (salicylic acid) or its sodium salt (sodium salicylate). Even though salicylic acid also has anti-microbial properties, the ingredient is mainly used for its keratolytic effects. Thus, it is particularly considered for use in combination with one or more of the other anti-fungal anti-dandruff actives.

The US FDA monograph for dandruff control requires salicylic acid to be used as an active only in the form of the acid, with approved dosages ranging from 1.8 to 3% [33]. In other regions where such an obligation is not given, often its salt (sodium salicylate) is used, mainly due to advantages in formulating, since sodium salicylate has good water solubility. Salicylic acid will then indirectly reach its acid form only in the formulation when shampoo pH is adjusted to <7 using citric or lactic acid.

In the EU market, anti-dandruff shampoos may also use up to 3% of the acid excluding use on children under the age of 3, while for other applications dosages of either max. 0.5 or 2% apply as per EU cosmetic regulation Annex III entry 98 and Annex V entry 3 [34].

China regulates salicylic acid similarly to the EU; thus, the ingredient is both listed in "*Restricted Ingredients Used in Cosmetics*" and in "*Permitted Preservatives Used in Cosmetics*". While, for non-preservative use, maximum dosages of 3.0% (hair rinse-off products, i.e., anti-dandruff shampoos) and max. 2.0% (leave-on products and skin rinse-off products) apply, it is not allowed in products for children under the age of 3 except for shampoo. If for preservative purposes, the limit of salicylic acid and its salts is 0.5% in total (calculated as acid), again except for shampoo, and it is not allowed in products for children under the age of 3. On 12 January 2026, China's NMPA officially implemented its revision on salicylic acid's use levels effective 1 January 2028, putting into force identical limits to those applicable in the EU.

Salicylic acid and its esters have widespread cosmetic use and have been subject to repeated safety assessments. The European Commission's Scientific Committee on Consumer Safety (SCCS) published its safety assessment in 2019 [60] with the following statements: Salicylic acid is safe as a preservative up to 0.5% in cosmetic products generally excluding oral care products (except lipsticks) and sprayable products subject to inhalation exposure. Salicylic acid is also considered an eye irritant with the potential to cause serious damage to the eye. Based on the data provided and available literature, the SCCS also considers salicylic acid safe when used for purposes other than preservation at a concentration up to 3.0% for cosmetic rinse-off hair products and up to 2.0% for other products. However, in body lotion, eye shadow, mascara, eyeliner, lipstick and roll-on deodorant applications, salicylic acid is considered safe only up to 0.5%. The SCCS position is that these levels are inclusive of any use of salicylic acid, i.e., they should not exceed the stated levels with additional use as a preservative. Salicylic acid is also used outside cosmetics, i.e., in pharmaceutical formulations such as anti-acne products. Such uses were not considered for aggregated exposure scenarios. Therefore, the actual total exposure of the consumer may be higher than exposure from cosmetic products alone. The conclusion of this opinion refers only to salicylic acid and not to other salicylates or salicylic acid salts. This assessment is the basis for today's use restrictions implemented in the EU cosmetic regulation [34].

In the US, in 2019 the Cosmetic Ingredient Review Expert Panel (CIR) also reviewed the safety of salicylic acid and 17 salicylates [61]. CIR concluded that salicylic acid is safe in cosmetics in the present practices of use and concentration described in the safety assessment when formulated to be non-irritating and non-sensitizing, which may be based on a quantitative risk assessment. On their list of ingredients reviewed, salicylic acid was assigned the second greatest frequency of use after ethylhexyl salicylate.

2.4. Hexamidine Diisethionate

2.4.1. Chemistry/Pharmacology

Hexamidine is a strong organic chemical base from the dibenzamidine group (chemical formula: $C_{24}H_{38}N_4O_{10}S_2$). Hexamidine (CAS 3811-75-4) and its predominantly utilized diisethionate (CAS 659-40-5) are used in cosmetics as anti-bacterial agents, disinfectants, and preservatives, up to a maximum concentration of 0.1%. Hexamidine diisethionate is an ethanol-soluble cationic substance. At elevated temperatures it also dissolves in water and propylene glycol but is insoluble in oils and fats. In terms of dandruff control, the white to slightly yellow hygroscopic powder is mainly used in rinse-off shampoo applications [62].

2.4.2. Mode of Action

Hexamidine has been shown to affect biomarkers of skin barrier function, such as corneocyte size and maturity, affect lipid biosynthesis and uptake, increase stratum corneum thickness, reduce trans-epidermal water loss (TEWL) and modulate the activity of serine proteases associated with inflammation and turnover of the skin [62].

The exact mechanism of anti-bacterial efficacy is still unclear [62] It is thought that hexamidine diisethionate binds with high affinity to the negatively charged cell walls and membranes of bacteria, inducing perturbations and leakage. In this sense, it may be considered a cationic surface-active agent [63].

Hexamidine diisethionate can cause allergic skin reactions [64,65]. Several cases of allergic contact dermatitis have been reported with hexamidine and in one case a systemic reaction was observed due to topical application [62].

2.4.3. Efficacy and Influence on Microbiome

Hexamidine diisethionate has been reported to be effective against *Pseudomonas aeruginosa, Proteus, E. coli, Staphylococcus aureus* and *C. albicans* [62,66]. The influence on the human cutaneous microbiota has been investigated with different results: Marked disturbance was reported by Michel et al. [67] whereas only slight modifications of the bacterial population were seen by Chevalier and Cremieux [68].

2.4.4. Ecotoxicology

Environmental Fate and Distribution

Hexamidine diisethionate was concluded to not be biodegradable in a biodegradability study (Table 1). The experimentally determined log Kow value of 4.47 is above the cut-off value of 4 (criterion for bioconcentration in aquatic organisms) and slightly below 4.5 (criterion for B). However, QSAR calculations predicting the bioconcentration factor (BCF) show that all predicted values are below the criterion for bioaccumulation potential (BCF < 500) [11]. Based on the predicted log Koc value of 5.07, hexamidine diisethionate can be considered as not mobile in soil [11,12].

Aquatic Toxicity

The number of ecotoxicological studies performed with hexamidine diisethionate is low [17]. Acute study results are only available for *Daphnia* and algae. No experimental long-term toxicity data are available for fish, *Daphnia* and algae. The acute effect concentrations determined for *Daphnia* and algae indicate that hexamidine diisethionate is very toxic to aquatic organisms (Table 1).

The acutely very toxic properties of hexamidine diisethionate to aquatic organisms and the missing long-term toxicity data lead to an acute aquatic toxicity cat. 1 (H400) and a chronic aquatic toxicity cat. 1 (H410) classification according to the GHS classification scheme [31]. Hexamidine diisethionate does not fulfill the PBT/vPvB and PMT/vPvM criteria of the CLP regulation [11,12].

2.4.5. Market Aspects and Regulations

Hexamidine diisethionate is only found in very few cases in the global personal care market for dandruff control in the last 20 years. From 2013 to 2018 only four to seven new consumer items were identified annually featuring this ingredient according to Mintel GNPD. A first small increase to 13 was noted in 2019, then increasing to 18 variants by 2023 and 38 in 2024. Still, comparing to 626 for PO in 2024 these are relatively small numbers (see Figure 1).

Hexamidine diisethionate is not considered an active by the US FDA monograph for dandruff control [33]. The EU lists hexamidines by their chemical name *benzenecarboximidamide, 4,4′-(1,6-hexanediylbis(oxy))bis-, and its salts (including isethionate and p-hydroxybenzoate)*, in cosmetics regulation Annex V entry 47, defining a maximum use concentration of 0.1% [34]. This use level of up to 0.1% also applies in China, while all hexamidines in total need to be considered. From a chemical regulation perspective, hexamidine diiesethionate is EU REACH registered by only one registrant [14].

2.5. Selenium Sulfide/Sulfur

2.5.1. Chemistry/Pharmacology

For decades, sulfur and its derivatives have been used in dermatological therapy because of its broad-spectrum anti-microbial and immunomodulatory activities, for example, in scabies, pityriasis versicolor, psoriasis and atopic dermatitis [69]. Selenium sulfides are compounds of sulfur and selenium. Selenium disulfide is known in cosmetic products by its INCI selenium sulfide (CAS 7488-56-4). However, after production via conventional synthesis methods, the individual compounds exist as a mixture of substances, which is often also called selenium disulfide due to the average ratio. It is a light orange to reddish-brown powder, insoluble in water, and has a melting point of <100 °C. When exposed to acids, toxic and highly odorous (rotten egg) hydrogen sulfide vapors are formed [69]. Selenium sulfide is a component of anti-dandruff shampoos due to its fungicidal and dandruff-removing properties [69]. These usually contain 1% of the active ingredient. Higher concentrations typically require a prescription.

2.5.2. Mode of Action

Selenium sulfide reduces cellular adhesion in the stratum corneum and also has anti-bacterial and mild anti-fungal activity, which may contribute to its effectiveness. Its anti-mitotic mechanism of action results in a reduction in the turnover of epidermal cells [7]. In vitro, selenium sulfide precipitates and denatures proteins of dermatophytes, which cause superficial mycoses in humans and animals [70]. Since selenium sulfide is not absorbed, there is no risk of poisoning if the preparations are used correctly. Side effects may include: Unusual oiliness or dryness of hair or scalp, increase in normal hair loss and scalp discoloration [71].

2.5.3. Efficacy and Influence on Microbiome

In a comparative study, ketoconazole (2%) and selenium sulfide (2.5%) were equally efficacious but ketoconazole proved to be better tolerated [72]. Turcu et al. reported on the efficacy of a SeS_2-based shampoo applied two to three times per week for 4 weeks in 1407 adult subjects [73]. At the end of the study all clinical signs had significantly ($p < 0.001$) improved. Tolerance was good or very good in 98.8% of the subjects. In addition to clinical effects, the Clavaud research group investigated the effect of selenium sulfide on the scalp microbiome in several studies [74–77]. In summary, selenium sulfide rebalanced the scalp microbiome and improved sebum quality by reducing peroxided squalene and optimizing the ratio of triglycerides/free fatty acids independent of the hair type. Furthermore, it was able to reduce the time-to-relapse of moderate-to-severe SSD flares after initial treatment with topical corticosteroid/salicylic acid or ketoconazole.

2.5.4. Ecotoxicology

Environmental Fate and Distribution

Selenium sulfide is an insoluble inorganic substance consisting of two naturally occurring elements, selenium and sulfur [78,79]. Both elements are nutritionally required by organisms (selenium as an essential micronutrient [78] and sulfur as a macroelement [79]).

In screening studies for biodegradation, log Kow or log Koc tests are designed to conclude on the environmental fate and distribution of organic substances, but studies with selenium sulfide have not been performed [18]. However, it is known that selenium can be bioaccumulated in aquatic food chains up to concentrations leading to toxic effects [78]. Regarding mobility it is expected that selenium sulfide has a low potential for adsorption [18].

Aquatic Toxicity

The available short-term toxicity study results for fish, *Daphnia* and algae mentioned in the REACH registration dossier of selenium sulfide indicate harmful effects only to fish (Table 1). However, selenium can accumulate and be biologically magnified to toxic levels in fish, causing, for example, severe reproductive failure even though waterborne concentrations are in the low microgram per liter range [78]. Based on this fact, some years ago EPA applied a four-part criterion with defined threshold values for selenium in different fish tissues and freshwater compartments to protect freshwater aquatic life [80].

Selenium sulfide has a legal classification as aquatic acute 1 (H400) and aquatic chronic 1 (H410) according to the CLP regulation [11] despite the fact that short-term toxicity study results in the REACH registration dossier do not reflect this classification [18].

2.5.5. Market Aspects and Regulations

Selenium sulfide is only found in a few cases in the global personal care market for dandruff control in the last 25 years. From 2000 to 2015 only 0 to 13 new consumer products were identified annually featuring this ingredient, according to Mintel GNPD, depending on the year. While a small increase to 20 was noted in 2016 it was not sustained over the following 6 years. Only in 2023 did a sudden jump to 28 products happen, followed by 71 items identified in 2024. This compares to 626 market products featuring PO, launched in 2024, and only 15 featuring sulfur according to Mintel GNPD (see Figure 1). It is likely that sulfur's properties do not match formulators' and consumers' expectations and, if so, sulfur is more likely applied in the form of selenium sulfide today. On the one hand the recent increase in selenium sulfide can be explained by the global need for alternative options to ZPT in non-EU markets and, on the other hand, by selenium sulfide's positive listing in the US FDA monograph for dandruff control.

The US FDA monograph requires a concentration of 1% active content for regular selenium sulfide or 0.6% for a micronized grade. Sulfur is also positively listed as an active ingredient for the control of dandruff by the FDA, requiring its dosage to be in a range from 2 to 5% [33].

In the EU, selenium compounds are generally banned from cosmetics except SeS_2 (cosmetics regulation Annex II entry 297). Selenium sulfide is permitted if used up to 1% specifically in anti-dandruff shampoo (cosmetics regulation Annex III entry 49), requiring detailed labeling as follows: *Contains selenium disulphide. Avoid contact with eyes or damaged skin* [34].

Similarly selenium sulfide is also China-compliant but approved only to be used exclusively in anti-dandruff shampoo up to 1%.

Sulfur is not specifically regulated in Europe or in China and thus can be considered an existing and permitted cosmetic ingredient in both markets.

Renowned brands still use selenium sulfide for shampoos targeting rather severe forms of dandruff. For example, Procter & Gamble's *Head & Shoulders Selenium Sulfide Dandruff & Seborrheic Dermatitis Shampoo* was relaunched in the US market in August 2025 featuring claims like *clinical strength* and *our maximum dandruff protection* and listing 1% selenium sulfide active content [81]. Vichy's (L'Oréal) *Dercos Technique Anti Dandruff DS Dermatological Shampoo* works with a combination of selenium sulfide and salicylic acid.

The Vichy shampoo can be identified globally, for example, in various European countries, i.e., the variant identified in the Norwegian market in July 2025 was manufactured in the EU, in Spain [82].

Yet, an unpleasant appearance and odor associated with selenium sulfide has been published in applied cosmetic journals [83].

From a chemical regulation perspective, SeS2 is EU REACH registered with three registrations in place [14].

2.6. Propanediol Caprylate/Propanediol Undecylenate

2.6.1. Chemistry/Pharmacology

PMC (CAS 102731-54-4) is a new cosmetic concept launched onto the market in 2020. PMC is an odorless, colorless and liquid ester that is easy to incorporate into shampoo formulations [6].

PMU (CAS 176504-44-2) is a cosmetic ingredient which has a similar mode of action to PMC. It is also an odorless, colorless liquid ester that is easy to incorporate into cosmetic formulations [6].

2.6.2. Mode of Action

Short- to medium-chain fatty acids possess anti-microbial activities, but their practical use in cosmetics is limited due to their intense smell and other technical disadvantages [84]. For this reason the corresponding esters with excellent skin compatibility have been developed for topical use. The ester is rapidly cleaved by *Malassezia* hydrolases in the external milieu, thereby releasing the free fatty acids caprylic acid or undecylenic acid as active agents. In vivo, this is postulated to result in an autoregulation of the *Malassezia* population dependent on the yeasts' density. If the ester is not hydrolyzed it acts as a conditioner and refatting agent [85].

2.6.3. Efficacy and Influence on Microbiome

In an agar dilution test PMC demonstrated minimum inhibitory concentration (MIC) values ranging from 500 to 1000 ppm for the dandruff-associated species *M. globosa* and *M. restricta*, which are in a similar range to those of caprylic acid [85]. PMU also exhibited anti-fungal activity against these species, with MICs of 1000–2000 ppm for *M. globosa* and 1000 ppm for *M. restricta*. For comparison, undecylenic acid showed MICs varying from 300 to 2000 ppm for *M. globosa* and 500 ppm for *M. restricta*. A small difference has been observed between the MIC values of undecylenic acid and its ester, PMU. Nevertheless, the anti-fungal efficacy inherent in the acid can be effectively achieved through the application of its ester, with the added advantage of the ester being an easy-to-handle liquid product. Both PMC and PMU are even effective in the case of azole resistance, as shown in azole-resistant strains of *M. pachydermatis* [39]. Lastly, like most anti-dandruff actives in the market, PMC and PMU both show effects against *S. aureus* which is reflected in their MIC of 500 ppm each [6].

PMC and PMU have been proven to be efficacious in numerous in vivo studies for cosmetic applications [6]. This includes studies showing PMC's effectiveness vs. control for both shampoo and leave-on application, indicating improvements towards heathier ratios in the bacterial scalp microbiome. PMC has also demonstrated effectiveness for dandruff control comparable to conventional benchmarks like climbazole [84] or PO. In a combination study, PMC and PO showed benefits over using PO alone [86]. Similarly, a combination of PMC with salicylic acid improved anti-dandruff effectiveness even at a lowered concentration of salicylic acid, compared to salicylic acid alone at the US FDA's approved maximum level [54]. Lastly PMU was found as effective as PMC in a sham-

poo study at identical use concentrations, with both esters providing a lasting dandruff reduction even during wash out [6].

Furthermore, the effects of PMC on skin barrier integrity were investigated in an unpublished in vivo study conducted by the manufacturer involving 20 pre-selected volunteers with dry scalp [87]. The objective was to assess the efficiency of a combination of PMC with PO on TEWL, a key indicator of skin barrier function, measured instrumentally using an open chamber method [88]. Participants applied a test shampoo for 14 days. One group used a shampoo containing 0.75% PO, while another group used a combination formulation containing 0.5% PMC and 0.25% PO. After 42 days (D42) of application, the group treated with 0.75% PO alone showed an increase in TEWL of +7% compared to baseline (D0), indicating a slight deterioration of the epidermal barrier (Figure 2). In contrast, the group treated with the combination of 0.5% PMC and 0.25% PO exhibited a decrease in TEWL of −12% (a surrogate endpoint for skin barrier function) from baseline. This suggests an improvement in dry scalp health (Figure 2).

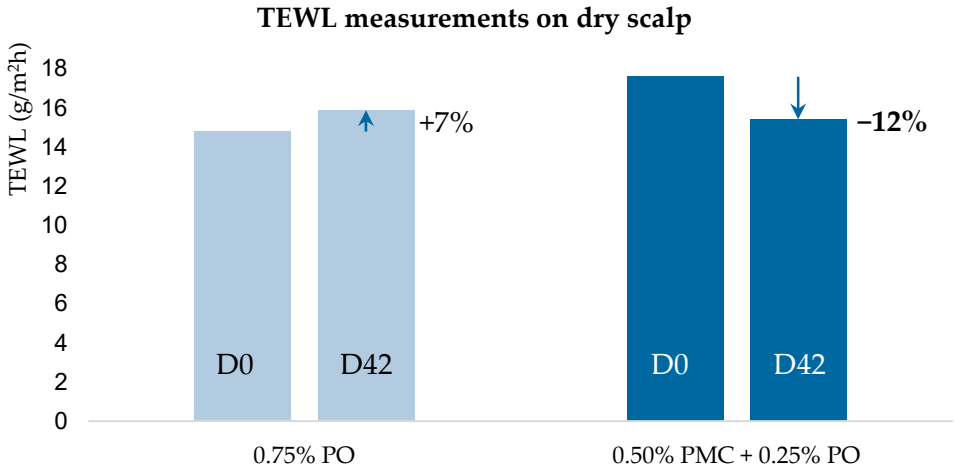


Figure 2. TEWL at the beginning and after 42 days of use of the investigational products containing either 0.75% PO or a combination of 0.5% PMC and 0.25% PO. The bars indicate means and percentage of reduction [87].

2.6.4. Ecotoxicology

Environmental Fate and Distribution

PMC and PMU as a new generation of anti-dandruff active ingredients are both readily biodegradable (Table 1). Based on the experimentally determined log Kow of 3.83 (25 °C and pH 10) the bioaccumulation potential of PMC can be considered low (below the cut-off values for the criterion for bioconcentration and bioaccumulation in aquatic organisms [11,12]). For PMU a bioaccumulation potential cannot be excluded based on the experimental log Kow of 4.78. However, QSAR calculations predicting the bioconcentration factor (BCF) show that all predicted values are below the criterion for bioaccumulation potential (BCF < 500) [11,12]. For both substances, the predicted log Koc values indicate that both substances are mobile in soil (Table 1) and therefore fulfill the criteria for M and vM, respectively [11,12].

Aquatic Toxicity

Since PMC and PMU are new cosmetic substances, only a limited number of experimental ecotoxicity data are available. Therefore, missing acute experimental data were predicted by QSAR calculations (Table 1). For both substances the short-term effect concentrations for fish, *Daphnia* and algae are in the same range (LC50/EC50 values are between 1 and 10 mg/L), therefore both substances are considered as acutely toxic to

aquatic organisms. Long-term effect concentrations are only available for PMC (algae (EC10 = 0.12 mg/L)), showing harmful effects.

Considering all available experimental and predicted data, both substances must be classified in acute aquatic toxicity cat. 2 (H401) and in chronic aquatic toxicity cat. 3 (H411) according to the GHS classification scheme [31]. Due to their readily biodegradable properties PMC and PMU are neither potential PBT/vPvB nor PMT/vPvM substances [11,12].

2.6.5. Market Aspects and Regulation

PMC and PMU are non-regulated cosmetic ingredients launched to the cosmetic ingredients market in 2020 (PMC) and in 2024 (PMU) respectively [89]. Both propanediol monoesters are young cosmetic concepts, with PMC already present on the market as part of consumer products on all continents (see Figure 1). By 2025, the highest number of variants as per Mintel GNPD has been identified in Europe (74), followed by Asia Pacific (14) and Latin America (14). Additionally, in North America (5) and in the Middle East and Africa (2) products have been placed on hair care consumer shelves. All identified market samples are hair and scalp care products, including shampoos (72), hair treatments (20) and conditioners (17).

Both ingredients carry the same reported functions in the PCPC INCI monograph, namely *anti-dandruff* and *skin conditioning*. Neither PMC nor PMU is considered an active by the US FDA monograph for dandruff control and as of today neither of the two ingredients has been approved for the Chinese cosmetics market (IECIC). Both PMC and PMU have been notified to the Chinese chemical inventory IECSC in a small volume below one tonne per year by Symrise and both PMC and PMU are EU REACH registered by Symrise as the only registrant [14].

2.7. Decylene Glycol

2.7.1. Chemistry/Pharmacology

Decylene glycol (CAS 1119-86-4, IUPAC name Decane-1,2-diol) is a cosmetic emollient with some reported efficiency supporting dandruff control [90–92].

2.7.2. Mode of Action

Decylene glycol exhibits broad-spectrum anti-microbial efficacy, particularly against bacteria and fungi relevant to skin health, such as *Staphylococcus aureus* and *Malassezia* species. Its mechanism involves disrupting microbial cell membranes, likely by integrating into the lipid bilayer and altering membrane fluidity, leading to cell lysis. This property makes it effective in controlling scalp conditions like dandruff, where *Malassezia* overgrowth is a key factor [93].

2.7.3. Efficacy and Influence on Microbiome

The multifunctional emollient decylene glycol was reported to prevent scalp inflammation by controlling sebum and inhibiting yeasts like *Malassezia* which led to a reduction in dandruff, qualifying the ingredient for modern scalp care [90,92]. Additionally, decylene glycol shows broad mild anti-microbial properties against further yeasts (*Candida albicans*) and dermatophytes (*Epidermophyton floccosum*) but also Gram-positive (*Cutibacterium acnes*, *Staphylococcus aureus*, and *Staphylococcus epidermidis*) and Gram-negative bacteria (*Pseudomonas aeruginosa*) [91]. MIC values range from 28 ppm (*M. furfur*) to 450 ppm (*P. aeruginosa*). Both mild anti-microbial efficacy and sebum-reducing properties contribute to improve scalp and skin health, while the reduced sebum levels indirectly limit the growth of lipophilic yeasts and bacteria and the mild anti-microbial efficacy directly targets relevant microbes, thus ensuring their sustainable control.

In ex vivo and in vivo studies, decylene glycol has been shown to reduce sebum production and support a healthier scalp microbiome. The ex vivo study evaluated sebum reduction utilizing microdissected sebaceous glands from human skin explants. Quantification of total lipids and proteins by infrared spectroscopy showed that treatment with decylene glycol significantly reduced total lipid content. Specifically, 0.9 ppm decylene glycol led to a 13% reduction ($p < 0.001$) and 9 ppm decylene glycol to a 25% reduction ($p < 0.001$) in total lipids compared to an untreated control [91]. These findings were further supported by an in vivo study evaluating a gel containing 2% decylene glycol compared to a placebo on the facial skin of 20 male subjects aged 17–19 with oily skin. Applying the product using a half-side face technique, measurements were taken at baseline and 3 and 4 weeks. After 21 and 28 days, the gel with 2% decylene glycol demonstrated a statistically significant reduction in the number of inflammatory lesions (pimples/pustules) ($p < 0.05$) compared to placebo. Concurrently, a significant decrease in sebum content, measured by SEBUMETER, was also observed with the gel containing decylene glycol after 21 and 28 days ($p < 0.05$) relative to the placebo treatment, confirming its efficacy in managing oily and acne-prone skin [91].

2.7.4. Ecotoxicology

Environmental Fate and Distribution

Based on the result of a biodegradation study, decylene glycol is readily biodegradable (Table 1). Furthermore, decylene glycol can be considered as not bioaccumulative, since the experimentally determined log Kow value (Table 1) is below the cut-off for bioconcentration and bioaccumulation in aquatic organisms [11,12]. However, the calculated log Koc value of 1.2 indicates a high mobility in soil, fulfilling the criteria for very mobile according to the CLP regulation [11,12].

Aquatic Toxicity

Acute toxicity data with decylene glycol are available for all three trophic levels (Table 1). The results indicate that decylene glycol is acutely harmful for fish, *Daphnia* and algae. Experimental aquatic long-term toxicity data are only available for algae, showing no toxic long-term effects (Table 1).

In summary, decylene glycol only shows acute harmful effects on aquatic organisms. Therefore, it is only classified as acute aquatic toxicity cat. 3 (H402) and is not classified for chronic aquatic toxicity [31]. Since decylene glycol is readily biodegradable, it is neither a potential PBT/vPvB nor a PMT/vPvM substance although the mobility criteria are fulfilled [11,12].

2.7.5. Market Aspects and Regulation

Decylene glycol is a non-regulated multifunctional cosmetic ingredient already present in the global market for dandruff control, with consumer products detected in all three reported markets, namely in the US [94], in Europe [95] and in China [96]. As a cosmetic ingredient, it is not considered as an FDA-approved active by the US monograph for dandruff control [33]. Decylene glycol with its multifunctional nature supports concepts for dandruff control and therefore can be considered as a combination partner for other anti-dandruff actives, rather than being considered a main active itself. For this reason, it is also found in pre-blended combinations for dandruff control [97]. From a regulation perspective the ingredient is China-approved (IECIC+IECSC) and EU REACH registered by the lead registrant Symrise with only one additional co-registrant [14].

2.8. Coal Tar

2.8.1. Chemistry/Pharmacology

Coal tars (CAS 8007-45-2) are highly complex mixtures of molecules, produced as a by-product in coke and coal gas manufacturing. They contain aromatic hydrocarbons, phenols, and heterocyclic compounds. Coal tars are viscous, dark, and have a strong odor, with notable anti-microbial and keratolytic properties in dermatological applications.

2.8.2. Mode of Action

The therapeutic effects of coal tar in skin disorders are attributed to keratolytic (comparable to salicylic acid) and direct and indirect anti-microbial properties: Coal tar slows down the growth of keratinocytes, a central side effect of psoriasis and dandruff, most probably due to its ability to suppress DNA synthesis and mitotic activity in the epidermis. Thus, it normalizes the cell turnover and reduces scaling. Coal tar also exhibits anti-microbial activity, particularly against fungi and bacteria implicated in scalp disorders. Phenolic and polycyclic aromatic constituents can disrupt microbial cell membranes and inhibit the growth of microorganisms. Additionally, coal tar has been discovered to activate the aryl hydrocarbon receptor, leading to the production of anti-microbial peptides generated from keratinocytes, thus creating an anti-microbial environment that is less susceptible to infection and inflammation in general [98]. Despite its efficacy, coal tar use has declined due to concerns about its physicochemical properties (odor, staining potential), as well as regulatory and toxicological considerations.

2.8.3. Efficacy and Influence on Microbiome

Due to its complex mixture and often varied components, specific microbiome studies on coal tar use are scarce. However, it was found that the application of coal tar cream can reduce the amount of *S. aureus*- and *S. capitis*-like strains in atopic dermatitis patients, whereas *Propionibacterium* levels increased [98]. Interestingly, the treatment did not reduce *S. aureus* specifically, thus demanding further studies with increased resolution regarding the specific microbiome composition.

2.8.4. Ecotoxicology

Coal tars are complex mixtures of hydrocarbons (mainly aromatic), phenolics, and heterocyclic oxygen, sulfur and nitrogen compounds. Experimental environmental fate and ecotoxicity studies for whole mixtures are rare. Furthermore, due to the complex interaction of components within the mixtures, it is difficult to predict the fate and toxicity of coal tars [99]. However, available literature data indicate toxic aquatic properties [22]. Since coal tars are of less importance as anti-dandruff actives the ecotoxicological profile was not further assessed.

2.8.5. Market Aspects and Regulation

Despite its positive listing by the US FDA monograph for dandruff control, coal tar is almost non-existent in the personal care market for dandruff control today. On the one hand, coal tar's physicochemical nature does not match formulators' and modern consumer expectations, while a coal-tar-type odor was positively associated with medicated efficacy in the past [83]. On the other hand, this ingredient is not a substantial option today, not even for the FDA-regulated US market due to toxicological and regulatory considerations.

The US FDA monograph still positively lists coal tar as an active ingredient for the control of dandruff, requiring its dosage to be in a range from 0.5 to 5% [33].

In Europe, the EU cosmetic regulation bans its use in personal care via Annex II (list of substances prohibited in cosmetic products) entry 420, listing crude and refined coal tars.

Similarly, the Chinese NMPA also prohibits the ingredient's use via their STSC [35].

3. Combination of Cosmetic Anti-Dandruff Active Ingredients

Many commercially available anti-dandruff products combine multiple active ingredients to address the multifaceted nature of the condition, often targeting both fungal activity and scalp inflammation [1–5]. A combination of actives is also advantageous from a consumer point of view, considering that distinguishing the exact nature of the condition, i.e., dry scalp vs. oily scalp, may not always be obvious.

Schmidt-Rose et al. reported that a combination of PO (0.5%) and climbazole (0.45%) proved to be equally effective in comparison with ZPT (1%) alone [100]. Ergin et al. assessed the efficacy of various PO and climbazole formulations against *Malassezia* sp. in comparison with ketoconazole. For all *Malassezia* sp. strains, climbazole 0.5% and PO/climbazole (0.1%/0.1% and 0.1%/0.5%) combinations were found to have the same effect as medicated shampoo containing 2% ketoconazole. A PO/climbazole 1.0%/0.1% formulation showed identical efficacy to 2% ketoconazole on *M. furfur* and *M. sympodialis*, while the 0.1%/0.5% formulation was only comparable regarding *M. furfur*. For *M. globosa*, none of the formulations tested was as effective as ketoconazole [101].

Considering salicylic acid as a keratolytic agent, a combination with additional ingredients to enhance shampoo effectiveness is advantageous. In a study by Loden et al. two shampoos with different actives were compared in a double-blind, randomized study on 19 subjects, the shampoo being applied twice weekly for four weeks [102]. One shampoo contained PO (0.75%) combined with salicylic acid (2%) and the other contained ZPT (1%) as active ingredients. The combination of PO and salicylic acid appeared to be slightly more effective than ZPT in reducing the severity and scalp area affected by the scaling.

Piérard-Franchimont et al. conducted a comparative study to evaluate the efficacy of a coal tar shampoo with salicylic acid (2%) and PO (0.75%). It was concluded in the study that non-coal-tar shampoo containing salicylic acid (2%) and PO (0.75%) yielded significantly greater reduction in dandruff [103]. Chen et al. evaluated the efficacy and acceptability of a 1% selenium disulfide (SeS_2) and 0.9% salicylic acid shampoo in treating mild to moderate SD thrice weekly for 4 weeks among 95 dermatologists. After the 4-week treatment, severe dandruff cases decreased from 28.4% to 3.2%, with 90.5% participants reporting only mild or no dandruff. Product satisfaction reached 88.5%, with 90.5% willing to recommend it clinically [104].

PMC was tested for synergistic effects in a randomized, double-blind study with a shampoo containing 0.75% PO versus a second shampoo containing 0.5% PMC plus 0.25% PO [86]. Both shampoos were applied at least three times a week. Although the PO positive control shampoo showed a slightly quicker scalp flaking decrease, no significant difference between the two treatments could be observed. A long-lasting effect was visible in the group of applicants of the combination. Here, the dandruff mean score continued its downward trend even in the wash-out phase (D63 vs. D42), while for the positive control shampoo an increase of the mean dandruff score from D42 to D63 in the direction of the initial value was observed. This indicates a particularly long-lasting effect for the ester.

In a further in vivo rinse-off shampoo randomized double-blind study two identical base formulations, one containing salicylic acid at its maximum dose of 3% and the second formulation featuring a reduced salicylic acid dose of 2% in combination with 0.5% PMC, were explored [54]. The actives combination reduced adherent dandruff by 32% while the positive control only showed a reduction of 21%. By the addition of PMC it is possible to reduce the dose of salicylic acid while observing an improved reduction of dandruff accompanied by an enhanced preservation effect. Furthermore, an improved overall sensorial performance of the product was observed for the shampoo containing this

ingredient combination. Recently we reported that using the new esters PMC or PMU in combination with PO increases PO's deposition onto the skin from rinse-off applications which is another clear benefit of using the combination of actives [105].

4. Discussion

The global cosmetic market for dandruff control is undergoing a huge transformation process (see Figure 1), and what we have seen so far is just the start. ZPT used to be the most used active globally but following the regulatory ban it has now been completely replaced in the EU. Other regional markets are discontinuing its use step by step and ZPT is expected to slowly disappear globally over time. On 12 January 2026 the Chinese NMPA officially introduced a ZPT ban effective from 1 January 2028.

Alongside PO and climbazole, the two main anti-fungal actives left in the cosmetics market, this review has also highlighted the entire list of actives (except ZPT) theoretically available as per the US FDA monograph for dandruff control. However, other than salicylic acid, most of them are not really viable for the consumer from a practical perspective which is obvious from their missing market presence shown in Figure 1. Only selenium sulfide is seeing some regrowth today, next to the non-US FDA-approved hexamidine diisethionate. An overview of the main anti-dandruff mechanisms for the ingredients covered in this review can be found in Table 3.

Table 3. Overview of the main anti-dandruff mechanisms of action as detailed in the text.

Ingredient	Anti-Fungal Activity	Anti-Bacterial Effects	Keratolytic Effects	Scalp Microbiome Modulation [1]
PO	+	Gram-pos. Gram-neg.	no data	*Malassezia* ↓ *Staphylococcus*↓ *Cutibacterium* ↑
Climbazole	+	Gram-pos.	no data	*Malassezia* ↓ *Staphylococcus* ↓
Salicylic acid/sodium salicylate	no data	Gram-pos. Gram-neg.	+	no data
Hexamidine diisethionate Diisethionate	+	Gram-pos. Gram-neg.	no data	no data
Selenium sulfide	+	Gram-pos.	+	*Malassezia* ↓ *Staphylococcus* ↓ *Cutibacterium* ↑
PMC/PMU	+	Gram-pos.	no data	*Malassezia* [2] ↓ *Staphylococcus* ↓ *Cutibacterium* ↑
Decylene glycol	+	Gram-pos. Gram-neg.	no data	no data
Coal tar	+	+	+	no data

[1] According to available literature, scalp microbiome modulation is considered a surrogate endpoint for anti-dandruff efficacy; [2] after activation by *Malassezia* enzymes; + = effects published.

Today PO has become the number one ingredient in Europe and globally (except for the US). We expect that this is a temporary situation in a dynamically changing market. With PO, manufacturers have opted for an established and easily accessible chemistry. There is no convincing evidence of a large gap between traditional and modern solutions in terms of safety and efficacy. However, all modern ingredients (PMC, PMU, decylene glycol) suffer from the fact that no independent efficacy studies are available currently. Despite

the six different in vivo studies published in peer-reviewed journals [6], most, if not all, data is derived from sponsored studies by the developer. This has created a considerable demand for the scientific community to compare and evaluate further, especially in regard to panel size and study duration. In the long run we expect that the market is going to focus even more on sustainability criteria. Chemistries like the new esters presented such as PMC and PMU could be favored. In more strictly regulated markets such as the US, there are different scenarios. Salicylic acid may become the main active, optionally used in combination with other technologies such as the esters for improved efficiency; or the market may go for products refraining from using claims like *dandruff control*.

From an environmental perspective the anti-dandruff active ingredients presented in this review show a broad spectrum of ecotoxicological profiles. An evaluation of the differences in the actual environmental impact may not be only based on the ingredient's intrinsic properties. Current hazard labeling varies mainly due to the different ecotoxicological data sets available. Generally a more comprehensive set of ecotoxicological data is available for older high-volume substances (e.g., PO, climbazole, salicylic acid) compared to those substances with low volumes that have only recently been launched to market; here especially long-term data is missing. A direct comparison of the environmental impact is limited due to uncertainties associated with the QSAR model, partially referenced predicted values and differences in available data.

In the context of sustainability anti-dandruff ingredients which are readily biodegradable like salicylic acid, PMC, PMU or decylene glycol have an obvious advantage over ingredients which are not biodegradable (e.g., PO, climbazole, hexamidine diisethionate), especially in combination with low toxicity (e.g., PMC, PMU, decylene glycol) or no toxicity for aquatic organisms (e.g., salicylic acid).

Finally, the importance of the scalp microbiome in dandruff pathogenesis should be further evaluated in methodologically standardized studies with a larger number of participants and extended application time with follow-up periods. Investigations on long-term safety, resistance development, and microbiome-focused outcomes should be included. The same applies to the best possible combination of active ingredients and the optimization of formulations.

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Abbreviations

The following abbreviations are used in this manuscript:

BCF	Bioconcentration factor (ecotoxicology)
CIR	Cosmetic Ingredient Review Expert Panel for Cosmetic Ingredient Safety (USA)
CLP	Regulation on classification, labelling and packaging, No. 1272/2008 (EU) [11]
EC10	10% effective concentration (ecotoxicology)
EC50	Half-maximal effective concentration (ecotoxicology)
ECHA	European Chemicals Agency (EU)
EPA	Environmental Protection Agency (USA)
FDA	Food and Drug Administration (USA)
FRSA	Fusidic-acid-resistant *Staphylococcus aureus*
GHS	Globally Harmonized System of Classification and Labelling of Chemicals
GNPD	Global New Products Database (Mintel)
IECIC	Inventory of Existing Cosmetic Ingredients in China
IECSC	Inventory of Existing Chemical Substances in China
INCI	International Nomenclature of Cosmetic Ingredients
LC50	Median lethal concentration (ecotoxicology)
log Koc	Organic carbon–water partition coefficient
MIC	Minimum inhibitory concentration
MRSA	Methicillin-resistant *Staphylococcus aureus*
NIFDC	National Institutes for Food and Drug Control (China, technical organization under NMPA)
NMPA	National Medical Products Administration (China, cosmetics authority)
NOEC	No observed effect concentration (ecotoxicology)
PBT	Persistent, bioaccumulative and toxic (ecotoxicology)
PCPC	Personal Care Products Council (USA)
PMT	Persistent, mobile and toxic (ecotoxicology)
PO	Piroctone olamine
PMC	Propanediol caprylate
PMU	Propanediol undecylenate
QSAR	Quantitative structure–activity relationship
REACH	Registration, Evaluation, Authorisation and Restriction of Chemicals, No. 1907/2006 (EU) [10]
SCCS	The European Commission's Scientific Committee on Consumer Safety (EU)
SD	Seborrheic dermatitis
STSC	Safety and Technical Standards for Cosmetics (China)
TEWL	Trans-epidermal water loss
US FDA	US Food and Drug Administration
vPvB	Very persistent and very bioaccumulative (ecotoxicology)
vPvM	Very persistent and very mobile (ecotoxicology)
ZPT	Zinc pyrithione

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