

Review

Artificial Intelligence in Cosmetic Formulation: Predictive Modeling for Safety, Tolerability, and Regulatory Perspectives

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Abstract

Artificial intelligence (AI) and machine learning (ML) are increasingly transforming the landscape of cosmetic formulation, enabling the development of safer, more effective, and personalized products. This article explores how AI-driven predictive modeling is applied across various components of cosmetic products, including surfactants, polymers, fragrances, preservatives, antioxidants, and prebiotics. These technologies are employed to forecast critical properties such as texture, stability, and shelf-life, optimizing both product performance and user experience. The integration of computational toxicology and ML algorithms also allows for early prediction of skin sensitization risks, including the likelihood of adverse events such as allergic contact dermatitis. Furthermore, AI models can support efficacy assessment, bridging formulation science with dermatological outcomes. The article also addresses the ethical, regulatory, and safety challenges associated with AI in cosmetic science, underlining the need for transparency, accountability, and harmonized standards. The potential of AI to reshape dermocosmetic innovation is vast, but it must be approached with robust oversight and a commitment to user well-being.

Keywords: artificial intelligence; cosmetic formulation; predictive modeling; computational toxicology; skin sensitization



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1. Introduction

In recent years, the field of cosmetic science has undergone a profound transformation, driven by technological advancements and evolving consumer expectations. Among these innovations, artificial intelligence (AI) has emerged as a disruptive force with the potential to revolutionize development, evaluation, and personalization of cosmetic products [1,2].

AI-based models are being explored not only to enhance formulation processes but also to anticipate safety profiles, optimize tolerability, and align with complex and evolving regulatory frameworks [3]. In fact, all cosmetic products—ranging from basic skin moisturizers to advanced anti-aging serums—are subject to stringent safety and efficacy standards [4,5]. In contrast to the pharmaceutical setting, clinical trials are generally not required prior to cosmetic market release. Nonetheless, cosmetics must comply with regulatory requirements in terms of safety, toxicology, and labeling, particularly in regions such as the European Union. Indeed, EU Cosmetic Products Regulation (EC) No.

1223/2009 mandates a comprehensive safety assessment prior to commercialization. Within this framework, predictive modeling offers an opportunity to transition from traditional, animal-based toxicology toward more ethical, cost-effective, and human-relevant testing strategies [6,7]. AI and machine learning (ML) tools can be trained on diverse datasets, including chemical structures, in vitro assay results, and historical safety data; as such, these instruments enable the simulation of biological responses and prediction of adverse effects with remarkable precision [8,9].

From an operational point of view, four primary ML paradigms are applicable in cosmetic formulation: supervised, unsupervised, semisupervised, and reinforcement learning [1,8]. Supervised learning relies on labeled datasets containing both input variables (e.g., chemical composition) and known outcomes (e.g., toxicity), enabling the model to learn predictive relationships [8]. While effective, this method depends heavily on large, high-quality labeled datasets, which are often costly and labor-intensive to produce. Unsupervised learning, in contrast, deals with unlabeled data, aiming to discover hidden structures or patterns, typically through clustering or dimensionality reduction [8]. Semi-supervised learning integrates both labeled and unlabeled data to enhance model performance when annotated data is limited. A notable approach within this framework is co-training, which employs multiple classifiers trained on distinct feature sets of the same dataset. Each classifier assigns pseudo-labels to the unlabeled data, which are then used to iteratively train the other classifiers. This mutual exchange of information improves predictive reliability through cross-validation and complementary learning dynamics [1,2]. Reinforcement learning (RL) introduces a different strategy, where an agent learns optimal actions by interacting with an environment and receiving feedback in the form of rewards or penalties [8]. While being promising in areas like robotics and recommendation systems, RL use in cosmetic formulation remains largely conceptual, with most studies limited to proof-of-concept stages [8].

The integration of AI into cosmetic formulation has also opened new avenues in ingredient discovery, formulation optimization, and consumer personalization [10]. Traditional formulation strategies, largely empirical and reliant on iterative testing, are being supplanted by data-driven approaches that leverage algorithms to predict ingredient compatibility, stability, sensory properties, and efficacy [11]. The aim of our work was to provide a comprehensive overview of emerging applications of AI in the cosmetic setting, with a particular emphasis on predictive modeling for safety, tolerability, and regulatory compliance.

2. Materials and Methods

Due to the narrative nature of the present review, no predefined inclusion and exclusion criteria were set prior to starting the evaluation of electronic sources. PubMed and SCOPUS electronic databases were used for our search. The key terms for our search strategy were “artificial intelligence” or “AI” or “machine-learning” or “in silico modeling” or “deep learning” and “cosmetics” or “cosmetic formulation” or “cosmetic ingredients. The database search was performed from inception to present. The following PICO (Population, Intervention or exposure, Comparison, Outcome) algorithm was applied in the present review: (i) Population: cosmetic products, (ii) Intervention: AI-based tools, (iii) Comparator: other possible tools or strategies for the development of cosmetics, (iv) Outcome: identification of the most important applications of AI in the cosmetological setting.

3. Results

From a comprehensive search on cosmetology and AI, we identified multiple reviews and clinical studies that collectively demonstrate AI’s ability to enhance diagnostic pre-

cision, customize cosmetic care algorithms, and improve patient satisfaction in cosmetic dermatology. Although publications on the intersection of cosmetics and AI remain relatively recent, there has been a noticeable increase in the number of studies over the past few years. Machine learning, in particular, plays a central role in applications such as personalized skincare recommendations, image-based skin analysis, and predictive modeling for cosmetic outcomes. Table 1 briefly presents the main ML models applied to cosmetic sciences.

Table 1. AI/ML Models Applicable to Cosmetic Science.

ML Paradigm	Description	Examples of Techniques	Applications in Cosmetology	Advantages	Limitations
Supervised Learning	Models are trained on labeled datasets (input + known output) to make predictions.	Support Vector Machines (SVM), Decision Trees, Regression	Prediction of toxicity, solubility, formulation stability, functional efficacy of ingredients	High predictive accuracy, suitable for well-defined endpoints	Requires large, high-quality labeled datasets; manual labeling effort is high
Unsupervised Learning	Models analyze unlabeled data to identify hidden patterns or groupings.	K-means Clustering, Hierarchical Clustering, PCA	Consumer segmentation, pattern detection in sensory and formulation parameters	Useful for exploratory analysis; autonomous pattern discovery	No direct output prediction; often less interpretable
Semi-supervised Learning	Combines small, labeled datasets with larger unlabeled ones to improve performance.	Self-training, Co-training	Enhancing model performance when labeled data are scarce; label propagation	Reduces labeling effort; improves generalization	Risk of error propagation with incorrect pseudo-labels
Reinforcement Learning	An agent learns optimal behavior through interaction with an environment and feedback (rewards/penalties).	Q-learning, Policy Gradient Methods	Adaptive formulation optimization; intelligent recommendation systems	Learns from experience; suitable for dynamic environments	Still mostly experimental in cosmetics; complex to implement in real-world scenarios

3.1. AI in Cosmetic Formulation

The integration of AI and ML in cosmetic formulation has extended beyond finished product development to encompass the design and optimization of individual cosmetic ingredients. This includes fundamental components such as surfactants, polymers, fragrances, and preservatives, each of which plays a pivotal role in the functional, aesthetic, and safety profile of cosmetic products [8]. Traditional approaches to ingredient development have often relied on trial-and-error experimentation and expert intuition. However, these methods are time-consuming, resource-intensive, and limited in their ability to explore vast chemical spaces. In contrast, AI-driven strategies allow for the virtual screening, prediction, and generation of new molecules with tailored properties, enabling rapid innovation while aligning with safety, sustainability, and regulatory constraints.

3.1.1. Surfactants

Surfactants play a crucial role in cleansing formulations, emulsions, and delivery systems, thanks to their amphiphilic nature, which facilitates the solubilization of lipophilic

substances, foam generation, and modification of skin feel (Table 2) [8,9]. Artificial intelligence techniques have been applied to both de novo design and property prediction of surfactants, with a focus on parameters such as critical micelle concentration (CMC), hydrophilic–lipophilic balance, toxicity, and biodegradability. Quantitative structure–activity relationship (QSAR) models, powered by supervised machine learning algorithms like random forests, support vector machines (SVR), and deep neural networks, have been trained on databases of known surfactants to predict key physicochemical properties and biological endpoints [12]. In a study by Boulkelkal et al., various machine learning approaches—including multiple linear regression, random forest regression, artificial neural networks (ANN), and SVR—were employed to develop quantitative structure property relationship (QSPR) models [13]. Additionally, generative models such as variational autoencoders and generative adversarial networks (GANs) have been used to design novel surfactant candidates with tailored solubility, foaming behavior, and environmental profiles [14]. Hamaguchi et al. analyzed over 500 samples to assess the cleansing performance of foam formulations [15]. Five machine learning models were evaluated, achieving a predictive accuracy of $R^2 = 0.770$. The study also employed virtual (in silico) formulations to identify promising ingredient combinations. The results underscored the nonlinear interactions among cosmetic ingredients, while also demonstrating that AI-assisted methods can effectively support the development of optimized cleansing formulations.

Table 2. AI applications in surfactant design.

Aspects	Features
Key Functions	Solubilization, foaming, skin feel [12]
AI Methods	QSAR, SVR, ANN, GANs [12–14]
Parameters Modeled	CMC, HLB, toxicity, biodegradability [13,15]
Data Sources	SMILES, 3D conformers, molecular descriptors [12,13]
Advantages	Virtual screening, de novo design, formulation optimization [12]
Limitations	Nonlinear interactions, data quality dependency [15]

3.1.2. Polymers

Polymers serve multiple roles in cosmetics, from viscosity modification and film formation to encapsulation and controlled release. Designing new polymers with targeted rheological behavior, sensory attributes, and environmental impact is a complex task, given the structural diversity and polydispersity of polymeric systems (Table 3). ML has shown promise in predicting polymer properties such as glass transition temperature (T_g), molecular weight distribution, solubility parameters, and tactile characteristics [16,17]. One emerging strategy is the use of graph neural networks (GNNs) and polymer-specific fingerprinting methods that account for repeating unit features, sequence information, and branching patterns. These models are trained on curated datasets linking polymer structure with functional outcomes in formulations [17]. Additionally, active learning approaches allow iterative refinement of models using data from high-throughput synthesis and rheology testing, closing the loop between prediction and experimentation. AI is also being used to support the design of biodegradable and bio-based polymers, which are increasingly important in the context of environmental regulation and consumer demand for “green” products [18,19]. Predictive models can assess polymer degradation pathways and potential environmental accumulation, aiding in the selection of monomers and polymer architectures that minimize ecological impact without compromising performance. However, in the context of cosmetic applications, machine learning-driven polymer design remains at an early stage of development [8].

Table 3. AI applications in Cosmetic Polymers.

Aspects	Features
Key Functions	Viscosity, film formation, delivery control [16,17]
AI Methods	GNNs, polymer-specific fingerprints, active learning [17–19]
Properties Modeled	Tg, solubility, MW distribution, feel [16–18]
Key Focus	Bio-based & biodegradable polymers [18,19]
Limitations	Sparse polymer-specific databases, insufficient fingerprints [8]
Potential	Eco-friendly formulations, sensory optimization [17–19]

3.1.3. Fragrances

Fragrance development is a multifaceted field at the intersection of chemistry, sensory science, psychology, and regulatory considerations. The olfactory profile of a cosmetic product plays a pivotal role in shaping consumer perception and emotional response; however, the design of fragrance molecules or blends has traditionally relied on the expertise of perfumers and empirical testing methods [20]. Artificial intelligence is transforming this landscape by enabling predictive modeling of odor characteristics and the automated creation of novel fragrance molecules (Table 4). Building on this innovation, Rodrigues et al. utilized GNNs to generate new odoriferous molecules aligned with consumer preferences [21]. Drawing on commercial fragrance databases, they employed k-means clustering to group perfumes according to shared sensory attributes, which in turn informed the GNN-based generation of new fragrance compounds. In another contribution, Santana et al. introduced a novel approach that integrates deep learning with simulation-optimization techniques [22]. Their method, based on a deep neural network (DNN), was trained using high-resolution simulation data and coupled with particle swarm optimization to identify the optimal composition of a four-component fragrance blend [22]. This technique effectively minimized undesirable odors while targeting a specific olfactory profile. Similarly, Zhang et al. proposed a computer-aided aroma design framework [20]. Their multi-step methodology began with the translation of desired product attributes into molecular constraints, followed by the construction of a structure–odor relationship model using ANNs. The framework was validated through experimental comparisons and case studies focusing on odor modulation and substitution. Computer-aided molecular design offers a powerful alternative by facilitating the identification of novel molecular structures with desired fragrance properties. A recent study by Heng et al. employed rough set-based machine learning (RSML) to develop interpretable models linking molecular structure and dilution levels to specific olfactory characteristics [23]. Finally, Mahmoud et al. tackled the challenge of incomplete sensory datasets through a deep learning approach called Alchemite [24]. This model outperformed traditional QSAR and graph-based techniques in predicting sensory properties, particularly in the presence of “activity cliffs,” and small structural changes result in significant shifts in perception.

Table 4. AI Applications in Fragrance Development.

Aspects	Features
Key Functions	Sensory appeal, emotional engagement [20]
AI Techniques	GNNs, ANN, DNN, RSML-CAMD [20–23]
Targets	Odor prediction, blend optimization, substitution [22–24]
Unique Aspects	Emotionally tuned blends, activity cliff prediction, odor constraints [22–24]
Benefits	Faster iteration, customized olfactory profiles [20,23,24]

3.1.4. Preservatives

Preservatives are essential for ensuring microbial safety and shelf-life of cosmetic products. However, increasing consumer awareness about potential health risks—such as sensitization, endocrine disruption, and neurotoxicity—as well as regulatory restrictions on substances like parabens, formaldehyde donors, and isothiazolinones—has created a strong demand for safer, more effective alternatives. AI models support the screening and design of new preservative agents by predicting antimicrobial efficacy, cytotoxicity, endocrine disruption potential, and sensitization risk (Table 5). AI-based tools support both the discovery and optimization of preservative agents by predicting antimicrobial efficacy, cytotoxicity, sensitization potential, and endocrine-disrupting properties [25]. Platforms such as DeepTox 2.0 and ProTox-II utilize deep neural networks trained on chemical and toxicological datasets to simulate interactions with biological targets, potentially reducing the need for in vivo testing and aligning with ethical standards such as the EU Cosmetics Regulation’s animal testing ban. ML algorithms can also enhance antimicrobial profiling by predicting minimum inhibitory concentrations (MICs) and identifying synergistic preservative mixtures that reduce the necessary concentration of each component, minimizing irritation and allergenic potential. For instance, Yan et al. employed a combination of terahertz spectroscopy and ML models to deconvolute multicomponent preservative mixtures, achieving a regression model with an R^2 of 0.989, thus enabling precise identification of composition even in complex matrices [26]. Moreover, AI facilitates toxicity prediction in early phases of development. Kan et al. developed a QSAR model using Random Forest and Synthetic Minority Over-sampling Techniques (SMOTEs) to predict neurotoxicity, achieving an accuracy of 87.7% when validated on an external set of 452 chemicals [25]. Out of 157 preservatives assessed, 15 were flagged as potentially cytotoxic to neuronal cells, demonstrating the potential of ML to pre-screen and prioritize compounds for further testing. Notably, AI is increasingly applied to the design of novel biomimetic antimicrobial peptides derived from human endogenous proteins. In a recent study, Yue et al. designed the AMP IK-16-1 based on human β -defensins using AI-driven peptide modeling [27]. This peptide demonstrated broad-spectrum antimicrobial activity against *Escherichia coli*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and *Candida albicans*, without exhibiting hemolytic activity—an essential criterion for cosmetic safety. AI tools predicted both antimicrobial and hemolytic properties, and experimental tests confirmed its efficacy and tolerability, suggesting IK-16-1 as a promising preservative synergist capable of reducing reliance on conventional preservatives.

Table 5. AI Applications in Preservatives Development.

Aspects	Features
Function	Antimicrobial protection, shelf-life extension [25]
AI Tools	DeepTox, ProTox-II, QSAR (RF+SMOTE), ML + spectroscopy
Target Outputs	MICs, cytotoxicity, EDC risk, neurotoxicity [25,26]
Innovation	Biomimetic AMPs, synergistic blends [27]
Advantages	Safety-focused screening, ethical compliance (no animal testing) [25–27]

3.1.5. Antioxidants

Antioxidant compounds are pivotal in combating oxidative stress and aging-related skin damage. Traditional antioxidant screening methods rely on extensive biochemical assays, which are both time-consuming and expensive. To streamline this process, Jung et al. developed ML models using a dataset of over 1900 compounds with experimentally validated antioxidant activities, achieving high classification accuracy with Random Forest and SVR models (>90%) based solely on chemical structures [28]. These models also per-

formed well on external validation using natural product datasets, indicating their potential for broad application in cosmetic ingredient discovery. Similarly, Lam et al. proposed a model to predict antioxidant proteins based on sequence-derived features, achieving an overall accuracy of 84.6%, with a sensitivity of 81.5% and specificity of 85.1% [29]. This approach demonstrates the value of ML not only in small molecule screening but also in identifying bioactive macromolecules with antioxidant function. Moreover, a hybrid method combining quantum mechanical calculations with ML has been shown to further improve predictive precision. Liu et al. presented a workflow where hydrogen atom transfer reactivity, a key mechanism in antioxidant action, was modeled using hydrogen dissociation energies derived from QM computations on flavonoid structures [11]. These values served as inputs for ML algorithms capable of screening thousands of candidate molecules efficiently, highlighting a promising direction for data-driven antioxidant discovery in cosmetics. By integrating these AI-driven techniques, the cosmetic industry can rapidly and accurately identify novel antioxidant ingredients, potentially reducing development time and improving the functional efficacy of final formulations (Table 6).

Table 6. AI applications in Antioxidant Ingredients development.

Aspects	Features
Function	Reduce oxidative stress, anti-aging [28]
AI models	QSAR, Random Forest, SVM, hybrid QM + ML [11,28]
Types	Small molecules, antioxidant proteins [11]
Application	Natural compound screening, reactivity modeling [11]
Benefit	Efficient high-throughput screening [11]

3.1.6. Prebiotics

The skin microbiome is essential for maintaining cutaneous immune balance and barrier integrity, with specific microbial communities adapted to distinct skin niches. Dysbiosis—characterized by an overgrowth of *Cutibacterium acnes* in acne or an increased abundance of *Staphylococcus epidermidis* and *Demodex*-associated bacteria in rosacea—has been linked to the onset and exacerbation of these inflammatory skin disorders [30]. Prebiotics are selectively fermented ingredients involved in microbiome modulation through the promotion of the growth of beneficial microorganisms. In the cosmetic field, their potential to rebalance dysbiotic skin microbiota and enhance skin health is increasingly recognized [31]. At the 78th conference of the Society of Cosmetic Chemists (SCC78 Conference), Jensen (Arcaea, LLC (Boston, MA, USA)) demonstrated a precision approach leveraging automation and ML to engineer microbiome-targeted prebiotics [11,32]. Two applications showcased the efficacy of this strategy: a deodorant enriched with prebiotics reduced underarm odor by altering microbial composition, while a prebiotic shampoo led to an 86% reduction in scalp flakiness and complete resolution of redness in clinical subjects, underscoring the potential of data-driven microbiome modulation for consumer benefits. Complementary evidence comes from studies applying explainable artificial intelligence to skin microbiome analysis [33]. Using leg skin microbiome samples from healthy women, researchers were able to predict phenotypic features such as skin hydration, age, menopausal status, and smoking behavior based on microbial signatures. This approach not only achieved accurate predictions but also identified key microbes responsible for phenotype variation, thus providing interpretable insights into host–microbiome interactions. Importantly, microbial shifts linked to hydration may inform the development of personalized skincare solutions aimed at optimizing barrier function and moisture retention (Table 7).

Table 7. AI-Driven Microbiome and Prebiotics Modulation.

Aspects	Features
Function	Rebalance microbiota, support skin health [11,30]
Outcomes	Odor control, dandruff reduction, hydration prediction [30–32]
Data Insights	Skin phenotype predictions (age, menopause, smoking) [32]
Potential	Personalized skincare, clinical efficacy mapping [32]

3.1.7. Texture and Sensory Perception

Beyond the selection of individual ingredients, the accurate prediction of a cosmetic product’s physical properties is crucial to its success. In contemporary cosmetic science, achieving the ideal combination of texture, stability, appearance, and overall pleasantness in topical formulations is both a creative pursuit and a data-driven process [34]. Texture—often described through rheological parameters such as storage modulus (G'), loss modulus (G''), yield stress, and thixotropy—plays a key role in shaping sensory perception, with specific rheological profiles associated with creaminess, reduced tackiness, and better spreadability [35]. In one study, these measurements were used as inputs to an artificial neural network (ANN) to predict consumer-rated sensory pleasantness, highlighting the value of data-driven approaches for texture optimization [36]. Appearance, including transparency, uniformity, and overall aesthetic quality, is also influenced by microstructure, as demonstrated by techniques such as small-angle X-ray scattering and photon correlation spectroscopy. For whitening creams, both texture and appearance are optimized to enhance consumer appeal and functional efficacy. Using a hybrid ANN–genetic algorithm model, Phuaksaman et al. demonstrated that computational optimization can predict melanin inhibition and identify precise active ingredient ratios to maximize efficacy while ensuring a pleasant, smooth finish [37]. Such findings illustrate how integrating machine learning with formulation science can align objective data with human sensory perception, ultimately improving product development and consumer satisfaction (see Table 8).

Table 8. Key findings on texture, appearance, and machine learning optimization in cosmetic formulations.

Aspect	Method/Model	Key Data/Performance	Reference
Texture parameters	Rheological measurements (G' , G'' , yield stress, thixotropy)	G' : 10–500 Pa; G'' : 5–200 Pa; Yield stress: 1–50 Pa; ANN model predicted sensory pleasantness with 60–84% accuracy	Calixto et al. [35], Franzol et al. [36]
Appearance and microstructure	Small-angle X-ray scattering, photon correlation spectroscopy	Transparent systems linked to finely dispersed droplets; milky emulsions linked to larger droplet sizes and higher phase separation risk	Roso et al. [34]
Whitening cream optimization	Hybrid ANN–genetic algorithm model	MSE: 6.01×10^{-4} ; R^2 : 0.979; Optimal actives: 3.00% Arbutin, 0.658% Aloesin, 0.007% Niacinamide, 0.993% Oxyresveratrol; Melanin content reduced to 0.0824; Sensory panel scores: >80/100 for smoothness and spreadability	Phuaksaman et al. [37]

3.1.8. Stability and Microstructure

Emulsion stability is closely linked to microstructure—whether oil-in-water (O/W), water-in-oil (W/O), or bicontinuous phases—which influence both visual clarity and shelf life. Differential scanning calorimetry (DSC) can be used to detect the state of water in different emulsion systems, providing insights into microstructural characteristics such as O/W, W/O, or bicontinuous phases [38]. In another study, researchers applied an artificial neural network (ANN) to predict microemulsion type based solely on composition,

demonstrating the feasibility of accurate classification using surfactant–cosurfactant ratios and component selection [39]. Additionally, deep-learning classification techniques have shown promise for assessing creams and gels by converting friction data from rub tests into spectrograms and applying convolutional neural networks (CNNs), which outperform traditional models and exhibit strong cross-validation robustness [40]. These findings suggest that instrument-based evaluations could complement or even replace conventional expert panels, enhancing formulation efficiency and consistency. Overall, such studies highlight the key role of texture and stability—measured through rheological and calorimetric analyses—and underscore the transformative potential of machine learning and optimization algorithms in refining cosmetic emulsions to meet both functional and sensory requirements. By integrating quantitative data and advanced neural networks, formulators can more precisely predict and adjust the tactile and visual qualities of creams and gels, leading to more efficient product development and improved consumer satisfaction (see Table 9).

Table 9. Summary of key findings on emulsion stability, microstructure, and machine learning applications.

Aspect	Method	Key Data/Performance	Reference
Microstructure detection	Differential Scanning Calorimetry (DSC)	- O/W: freezing peak of supercooled water ~−17 °C-Bicontinuous: bound-water peak ~−50 °C - W/O: lipid-phase solidification ~−8 °C; no water peak	Ravera et al. [38]
Prediction of microemulsion type	Artificial Neural Network (ANN) trained on 170 formulations	90% accuracy; surfactant–cosurfactant ratios of 1:1, 2:1, 1:2; 30–40 wt.% surfactant (Tween 40) and cosurfactant (glyceryl caprylate)	Gasperlin et al. [39]
Gel type classification	ResNet-based CNN with STFT spectrograms from rub test data	>90% accuracy; outperformed CWT-based 2D and 1D CNNs; robust across k-fold cross-validation	Sim et al. [40]

3.2. Predicting Efficacy, Toxicity, and Skin Tolerability Using In Silico Models

3.2.1. AI for Predicting Clinical Outcomes in Dermatology

Recent advancements in artificial intelligence have opened new frontiers in the prediction of treatment outcomes. While the diagnostic usefulness of AI in dermatology is well-established, with models achieving diagnostic accuracy akin to dermatologists, its predictive capabilities in therapeutic response and cosmetic satisfaction are now gaining scientific attention. AI predictive potential, encompassing both medical and aesthetic domains, could lead to optimization of treatment strategies, minimization of trial-and-error, personalization of cosmetic recommendations, and enhancement of patient satisfaction. The number of studies investigating ML-based prediction of clinical outcomes in dermatology remains limited but promising. According to a comprehensive review by Du et al., only six such studies were identified to cover diverse applications, ranging from risk stratification of chronic venous ulcers to likelihood estimates of treatment discontinuation in psoriasis patients [41]. Emam et al. applied multiple machine learning algorithms to a dataset of psoriasis patients to predict the risk of biologic therapy discontinuation, demonstrating the potential for individualized treatment planning and advancing the goals of precision dermatology [41–43]. Similarly, the use of deep learning models has proven valuable for risk stratification in non-melanoma skin cancer, as shown by Wang et al. and Roffman et al., highlighting the importance of dataset quality and feature selection in addition to sample size [43,44]. Further innovations include logic-based models: Khozeimeh et al. employed a fuzzy rule-based system to predict treatment responses in patients with warts, offering an interpretable approach that supports clearer communication between clinicians and patients [45]. Procedural dermatology has also benefited from these tools; Tan et al. com-

pared various algorithms to predict surgical complexity in periocular basal cell carcinoma excisions, aiding surgical planning and helping to manage patient expectations [46]. Key performance metrics for these studies are summarized in Table 10.

Table 10. AI Predictive Models for Clinical Outcomes in Dermatology. N/A: Not applicable.

Application	Study	Sample Size	Algorithms Used	Performance Metric	Notes
Psoriasis biologic discontinuation	Emam et al. [42]	681 patients	GLM, RF, ANN	AUC = 0.95	N/A
Non-melanoma skin cancer	Wang et al. [43]	9494 patients	Semi-supervised CNN	AUC = 0.89	Sensitivity: 83.1%, Specificity: 82.3%
Cryotherapy and immunotherapy response prediction in wart treatment	Khozeimeh et al. [45]	180 patients	Fuzzy logic	AUC = 0.902	Accuracy for cryotherapy: 80%, Accuracy for immunotherapy: 98%
Surgical complexity following periocular basal cell carcinoma excision	Tan et al. [46]	156 patients	Naive Bayesian classifier	AUC = 0.854	Positive predictive value: 38.1%, Negative predictive value: 94.1%

3.2.2. AI for Predicting Cosmetic Satisfaction and Consumer Behavior

The field of cosmetology has increasingly embraced AI for the prediction of aesthetic outcomes and user satisfaction. Unlike therapeutic interventions, cosmetic treatments often involve subjective expectations, variable preferences, and psychosocial factors. Here, AI’s ability to interpret complex, high-dimensional data such as emotional states, facial traits, and behavioral responses becomes especially valuable [3]. For instance, Kim et al. developed CNN models to predict user satisfaction with different cosmetic creams based on electroencephalography (EEG) data [47]. Participants’ brainwave activity was recorded during application of four creams differing in texture, and the CNN models—trained on features across alpha, beta, low gamma, and high gamma bands—achieved an average classification accuracy of 75.4% in distinguishing between “liked” and “disliked” products. This approach exemplifies the role of neurocosmetics, where emotional and sensory responses are quantified using biosignals to predict product compatibility and satisfaction. The application of AI in consumer behavior prediction has also evolved to include image-based systems for product simulation. Tong et al. were pioneers in virtual makeup transfer, using image transformation techniques to simulate cosmetic effects pixel-by-pixel [48]. More recently, Flament et al. developed an AI-based system capable of analyzing 23 facial traits from selfies, offering personalized makeup advice validated by a panel of twelve experts [49]. This model achieved high levels of user satisfaction across diverse demographic groups, confirming its utility in tailoring cosmetic recommendations to individual anatomy and preference [49]. Skincare outcomes, too, can be predicted using AI. Shi et al. developed “SkincareMirror,” an AI tool that forecasts changes in skin appearance after long-term use of cosmetic products by integrating user photos, product functions, and expected efficacy [50]. This tool proved especially beneficial for users with less skincare knowledge, enhancing informed decision-making and increasing satisfaction. In validation studies, male users with limited skincare experience demonstrated significantly greater confidence in their purchase decisions when using SkincareMirror compared to traditional methods [50]. In both medical and cosmetic domains, AI models are now being employed not only for analysis but also for visualization. In aesthetic dermatology, the “virtual try-on” concept is gaining traction [1]. By providing realistic previews of post-treatment appearance, AI helps

mitigate unrealistic expectations and improves patient satisfaction. Such technologies allow clinicians and consumers to engage in a collaborative, data-driven discussion about achievable outcomes, significantly enhancing transparency and trust in the treatment process. Moreover, these models can integrate multidimensional data—clinical features, emotional states, lifestyle inputs, and visual cues—to deliver holistic predictions. This multidimensionality is particularly important in dermatology and cosmetology, where patient response to topicals is influenced by a combination of biological, environmental, and behavioral variables. Deep learning models excel in capturing nonlinear interactions among these variables, thereby offering predictive outputs that are more nuanced and patient-specific than those derived from traditional statistical methods [1,3,51]. Despite these advances, some limitations persist. Many models require large, well-annotated datasets, which are not always available, particularly in cosmetic science where privacy and subjective response present unique challenges. In dermatology, national and international registries are beginning to address this gap, but continued collaboration and standardization are needed to enable broader deployment of AI tools. Additionally, while some models—such as fuzzy logic systems—offer transparency, others function as “black boxes,” raising concerns about interpretability and accountability. Clinician oversight remains crucial to contextualize AI-generated predictions within the broader clinical and psychosocial landscape of patient care.

3.2.3. In Silico Approaches for Acute Dermal Toxicity

Alongside the growing understanding of the molecular and cytokine-driven mechanisms underlying allergic contact dermatitis and skin toxicity, recent years have seen significant progress in the development of non-animal testing approaches for evaluating cutaneous reactions, particularly in the fields of cosmetic and pesticide safety [52]. Acute dermal toxicity and skin sensitization are two pivotal endpoints in toxicology, especially given their relevance for consumer products and occupational exposure [3,10]. Traditional assessment methods have long relied on *in vivo* testing in animals such as rabbits, rats, and guinea pigs. However, growing ethical concerns, regulatory changes—most notably the European Union’s complete ban on animal testing for cosmetic products and their ingredients since 2013—and scientific innovations have fueled the transition toward alternative methodologies [3]. Among these, *in silico* modeling, supported by ML and DL, is emerging as a powerful tool for predicting skin toxicity without the need for animal testing. Acute dermal toxicity refers to the adverse effects that occur following the application of a substance to the skin. Traditionally, determining the dermal toxicity of chemicals, such as active ingredients in pesticides or components in cosmetics, required extensive animal testing. However, such methods often present limitations in terms of ethical acceptability, cost, and translatability to human systems. To address these issues, researchers have begun to develop *in silico* models that leverage historical experimental data to predict dermal toxicity outcomes. In one such study, over 3400 animal-based data points were used to train ML and DL algorithms, achieving promising AUC scores of 78% for rabbit-based data and 82% for rat-based data in 10-fold cross-validation [53]. These models were further enhanced through tools like SARpy, which identifies structural alerts, and interpretability methods such as Shapley Additive Explanations and attentive fingerprint heatmaps. Together, these tools elucidate the key molecular features contributing to toxicity. The study culminated in the development of a standalone software tool designed to streamline the prediction of acute dermal toxicity, marking a step forward in regulatory and safety evaluations for cosmetics, pesticides, and pharmaceuticals.

3.2.4. Skin Sensitization Prediction and Industry Applications

Parallel efforts in the cosmetics industry have focused on predicting skin sensitization—an immune-mediated response manifesting as allergic contact dermatitis. Before the EU ban, the sensitizing potential of cosmetics and their ingredients was primarily assessed using animal models such as the Böhler Test, the Guinea Pig Maximization Test, and the Local Lymph Node Assay (LLNA) [10]. The LLNA used mice and measured lymph node proliferation in response to test substances. However, these methods are now largely replaced or complemented by a spectrum of New Approach Methodologies (NAMs), including *in vitro* assays (e.g., h-CLAT, DPRA, KeratinoSens) and *in silico* models [3,54,55]. *In silico* models for skin sensitization are constructed using diverse algorithmic approaches, including decision trees, ANNs, support vector machines, logistic regression, and Bayesian networks [55]. These models draw from extensive datasets such as those maintained in the Cosmetic Ingredient Database (CosIng) and the Cosmetics Europe database. Among the algorithms tested, the best-performing model was a Naive Bayes classifier trained on 24 physicochemical descriptors and eAR values, achieving an overall accuracy of 86%, sensitivity of 80%, and specificity of 90% [56]. This model was then applied to assess the sensitizing potential of 15 emerging or poorly studied haptens, of which 7 were predicted to be sensitizers: cyclamen aldehyde, N,N-dimethylacrylamide, dimethylthiocarbamyl benzothiazole sulphide, geraniol hydroperoxide, isobornyl acrylate, neral, and prenyl caffeate [57]. An alternative model using the Random Committee algorithm trained on 17 parameters and eOR data was also made available for further validation [10]. One prominent advantage of *in silico* models is their scalability and efficiency. They can rapidly screen large libraries of chemical compounds, identify potential sensitizers, and prioritize substances for further investigation. This facilitates more accurate safety margins and supports formulation decisions that minimize consumer risk [58,59]. These models also consider differences in exposure scenarios—such as the contrast between rinse-off products like shampoos and leave-on products like creams—providing context-specific risk assessments. A compelling case for the adoption of *in silico* models is their performance relative to both animal and human data. In collaborative efforts by Cosmetics Europe and the National Toxicology Program, multiple defined approaches were benchmarked using curated LLNA and human sensitization datasets [60]. The outcome demonstrated that these non-animal strategies, incorporating various computational and biological inputs, performed on par with or better than traditional methods [10]. Notably, these models did not consistently misclassify the same compounds, suggesting that ensemble approaches or consensus modeling could further enhance predictive reliability. Furthermore, software tools like the SpheraCosmolife package exemplify the integration of exposure and hazard prediction in cosmetic safety [54]. This platform provides safety assessments across different product types and concentrations, delivering a calculated Margin of Safety and helping manufacturers comply with regulatory frameworks [61]. Such tools also support the 3Rs principle—Replacement, Reduction, and Refinement of animal use—offering ethically responsible and scientifically sound alternatives [62]. Despite these advancements, challenges remain. The accuracy of *in silico* models is intrinsically tied to the quality and representativeness of the input data. Imbalanced datasets—with more known sensitizers than non-sensitizers—can bias model performance. To mitigate this, techniques such as data rebalancing and multi-class classification are being increasingly employed. Moreover, most current models focus on a limited number of adverse outcome pathways, often overlooking complex biological interactions and individual variability in human responses.

3.3. Model Performance Summary

Across all AI applications described, model performance metrics demonstrate robust predictive power for key formulation, safety, and efficacy endpoints. Predictive accuracies, R^2 values, AUC scores, and validation approaches are summarized in Table 11 for ease of reference. These results confirm that machine learning algorithms—from classical models like random forests and support vector machines to advanced deep neural networks and graph-based architectures—consistently deliver high performance when trained on well-curated cosmetic and dermatological datasets. Notably, these models have proven reliable across various sample sizes and cross-validation schemes, reinforcing their value for both ingredient design and product optimization.

Table 11. Overview of predictive performance metrics (R^2 , AUC, accuracy) for AI and ML models applied in cosmetic formulation, safety assessment, and clinical outcome prediction. N/A: not applicable. The downward arrows ($\downarrow$) indicate a reduction of the considered parameters.

Application Area	Sample Size/Data	Algorithm(s) Used	Key Metric(s)	Reference
Surfactants property prediction	>500 samples	MLR, RF, ANN, SVR	$R^2 = 0.77$	Hamaguchi et al. [15]
Microemulsion type classification	170 formulations	ANN	Accuracy: 90%	Gasperlin et al. [39]
Gel type classification	N/A	ResNet CNN with STFT	Accuracy: >90%; robust k-fold	Sim et al. [40]
Whitening cream optimization	Expert-derived dataset	Hybrid ANN–GA	$MSE = 6.01 \times 10^{-4}$, $R^2 = 0.979$	Phuaksaman et al. [37]
Rheology–sensory mapping	39 emulsions	ANN	Sensory pleasantness: 60–84%	Calixto et al. [35]
Prebiotics microbiome prediction	N/A	Explainable AI	Odor $\downarrow$, flakes $\downarrow$, redness $\downarrow$	Jensen et al., SCC78 [32]
Acute dermal toxicity (in silico)	>3400 data points (animal)	ML + DL + SARpy	AUC: 78% (rabbit), 82% (rat)	Lou et al. [53]
Skin sensitization prediction	157 substances (LLNA data)	Naive Bayes, Random Committee	Accuracy: 86%, Sens: 80%, Spec: 90%	Zhang et al. [20]
Clinical outcomes in psoriasis	681 patients	GLM, RF, ANN	AUC: 0.95	Emam et al. [42]
Non-melanoma skin cancer risk strategy	9494 patients	Semi-supervised CNN	AUC: 0.89	Wang et al. [43]
Wart treatment response prediction	180 patients	Fuzzy logic	AUC: 0.902	Khozeimeh et al. [45]
Surgical complexity in BCC excisions	156 patients	Naive Bayes	AUC: 0.854	Tan et al. [46]
User satisfaction (neurocosmetics)	EEG from cream tests	CNN	Accuracy: 75.4%	Kim et al. [47]
Skincare efficacy forecasting	N/A	“SkincareMirror” hybrid model	Higher user confidence scores	Shi et al. [50]

3.4. Ethical and Legislative Challenges

The integration of AI into dermocosmetic science introduces significant ethical and regulatory challenges, particularly in relation to algorithmic fairness, model transparency, and data governance. One of the most critical concerns involves algorithmic bias, often stemming from the use of non-representative datasets in model training. In the context of cosmetic science, datasets frequently overrepresent lighter phototypes, younger individuals, and specific gender expressions, leading to predictive outputs that lack generalizability and may perpetuate dermatological inequities [63]. This limitation not only undermines

clinical and commercial utility but may also contribute to the reinforcement of narrow aesthetic paradigms, ultimately marginalizing diverse user populations. Moreover, opacity in AI decision-making—commonly referred to as the “black box” problem—poses a substantial barrier to clinical and consumer trust. The absence of interpretable models impedes the ability of healthcare providers and cosmetic scientists to validate algorithmic outputs, potentially compromising decision-making processes [64,65]. This is particularly problematic in domains such as dermatological risk assessment or personalized skincare formulation, where explainability is essential to ensure both clinical accountability and user comprehension. In parallel, the widespread deployment of AI systems in dermocosmetics necessitates rigorous attention to data protection and cybersecurity [3]. These platforms often process highly sensitive biometric and behavioral data, including facial morphology, skin condition imaging, and digital behavioral traces. The collection, storage, and utilization of such data must comply with existing legal frameworks for personal data protection, such as the EU General Data Protection Regulation, while also anticipating emerging requirements under AI-specific legislation. A pivotal regulatory development in this context is the European Union’s Artificial Intelligence Act (AI Act), formally adopted in 2024 [66]. This legal instrument establishes a risk-based framework for the development, deployment, and monitoring of AI systems across multiple sectors, including health and consumer products. Under the AI Act, cosmetics AI applications may be classified as “high-risk” when used for diagnostic or treatment-related functions, thereby subject to stringent obligations. These include requirements for high-quality, representative training data; robust documentation and traceability mechanisms; transparency obligations; and the implementation of human oversight protocols. Importantly, the AI Act mandates that all AI systems conform to fundamental rights protections, including non-discrimination, data minimization, and the right to explanation, thereby reinforcing ethical imperatives within a legally enforceable structure. From an operational perspective, compliance with the AI Act will require interdisciplinary collaboration between cosmetic formulators, AI developers, clinicians, and legal experts to ensure algorithmic accountability, minimize systemic bias, and preserve user autonomy. Furthermore, manufacturers and developers must integrate ethical and regulatory compliance from the earliest stages of AI model design—an approach aligned with the principles of “ethics by design” and “privacy by design” [65,67].

4. Discussion

AI, particularly ML, represents a transformative paradigm in cosmetic science, with the potential to revolutionize how products are formulated, tested, personalized, and regulated. While early implementations have focused primarily on predictive modeling for safety and efficacy, the broader implications of AI span far beyond technical optimization.

From a practical standpoint, AI significantly enhances the speed, cost-efficiency, and reproducibility of formulation processes, contrasting sharply with the “trial-and-error” method (Figure 1).

Deep learning techniques, for instance, can analyze complex datasets to identify synergistic combinations of active ingredients or forecast solubility and emulsification potential, therefore potentially reducing time and costs of product development while simultaneously increasing formulation precision and reproducibility. Moreover, AI holds transformative potential in the assessment of product tolerability, which is particularly crucial for cosmetics intended for prolonged or repeated use [10]. Data-driven models reduce the need for iterative, trial-and-error experiments by enabling *in silico* screening of ingredients and prediction of critical formulation parameters (e.g., solubility, stability, rheology, texture). These methods support a “fail fast” approach, where suboptimal candidates can be excluded early in the pipeline, preserving time and resources. Moreover, AI can

accelerate the identification of safer, more sustainable ingredients, aiding in the transition from controversial preservatives and synthetic additives toward greener alternatives, such as biomimetic peptides, biodegradable polymers, and low-impact surfactants. This aligns with the principles of sustainable development and with rising consumer expectations for ethically produced cosmetics.

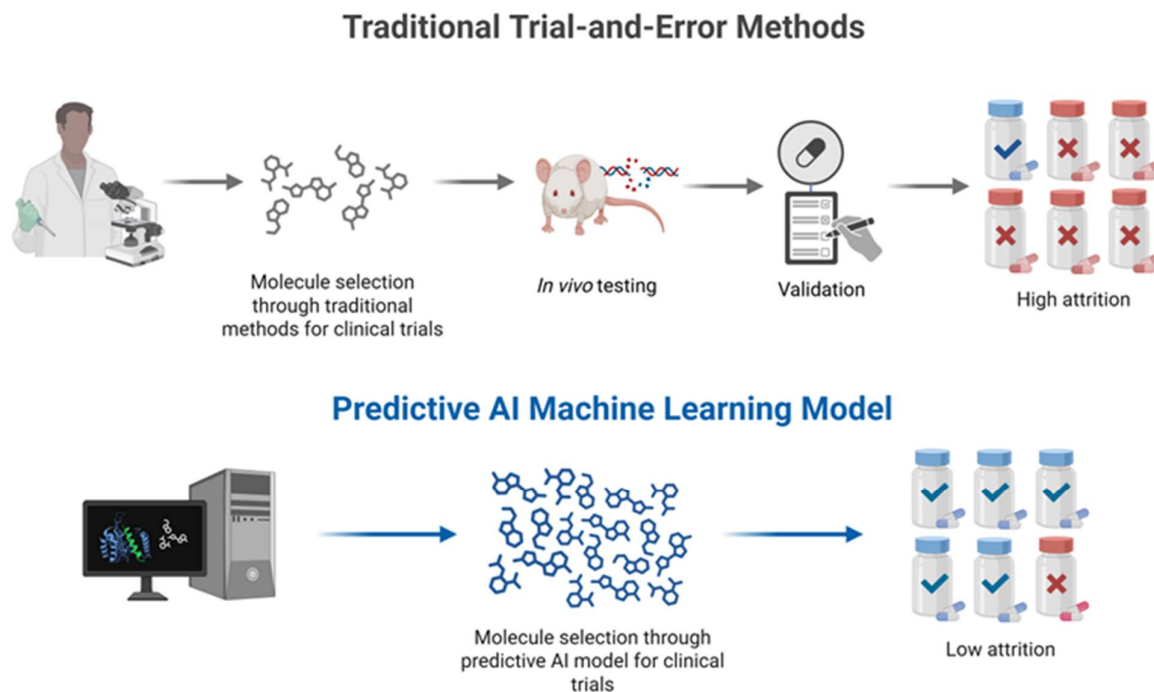


Figure 1. Traditional trial-and-error versus AI-driven predictive approaches in cosmetic formulation: (Above), the conventional method relies on empirical molecule selection, in vivo testing, and sequential validation steps, often resulting in high attrition rates and extended development timelines. (Beneath), the AI-based workflow employs predictive modeling and machine learning to identify promising compounds in silico, reducing experimental burden and increasing formulation efficiency with lower attrition. Created in BioRender. Di Guardo, A. (2025) <https://BioRender.com/8breoi4>, accessed on 1 July 2025.

Another key advantage of AI lies in risk mitigation and safety assessment. Adverse reactions, though typically less severe than those encountered in pharmaceutical settings, can significantly impact consumer satisfaction and product viability. Nowadays, ML models trained on clinical or genomic data and post-marketing surveillance can effectively be used for predicting skin irritation, allergic responses, or photosensitivity [68]. Predictive toxicology models, trained on historical datasets and validated against regulatory benchmarks, offer a viable alternative to animal testing, in full compliance with EU directives. When coupled with advances in wearable biosensors and digital dermatology, these technologies also facilitate real-time monitoring of tolerability in post-marketing phases [69,70], enabling transparent and reproducible safety evaluations, while promoting compliance with ethical standards and data protection regulations.

While regulatory bodies (such as the European Commission and the U.S. Food and Drug Administration) are already actively exploring the validation and standardization of in silico models in toxicology, official indications on AI-driven predictive models in the cosmetological setting are still lacking [71,72]. The absence of clear regulatory pathways may hinder the widespread adoption of AI tools, particularly in the context of risk assessment and product claims. To this end, collaborative initiatives involving industry, academia, and regulatory agencies are essential to define best practices, ensure transparency in algo-

rhythmic decision-making, and validate model performance across diverse populations and use scenarios [73–75].

The integration of artificial intelligence into the field of cosmetic science presents both substantial opportunities and significant challenges. On the one hand, AI offers transformative potential for the development of personalized formulations through the prediction of product performance, tolerability, and consumer satisfaction with unprecedented precision [2,8]. This technological capability supports the customization of skincare not only based on skin type or personal concern but also on variables such as age, hormonal status, lifestyle, ethnicity, and even microbiome composition [73–75]. The potential application of AI and ML in the formulation of dermocosmetic products for patients with skin diseases that have significant clinical and psychological impact, such as psoriasis and atopic dermatitis, is also of considerable importance [76,77].

Nevertheless, the societal and ethical implications of AI must not be overlooked. Algorithmic biases and privacy concerns demand proactive governance [17,18]. The cosmetics industry has for a long time promoted strict aesthetic standards, primarily favoring lighter skin phototypes and younger individuals. If unaddressed, AI may replicate and even amplify these biases. At the same time, AI may also represent an opportunity: by implementing strategies such as dataset diversification, algorithmic fairness techniques, and adherence to emerging regulatory frameworks, developers could build more inclusive and equitable systems. Lastly, the use of consumer data—frequently sourced from mobile apps, wearables, or social media—raises critical questions about privacy, consent, and transparency. Ethical stewardship in data governance is essential to ensure that these technologies remain consumer-centric and trustworthy. Addressing these challenges is crucial to ensure that AI applications benefit diverse populations and support fair and transparent decision-making (Figure 2).

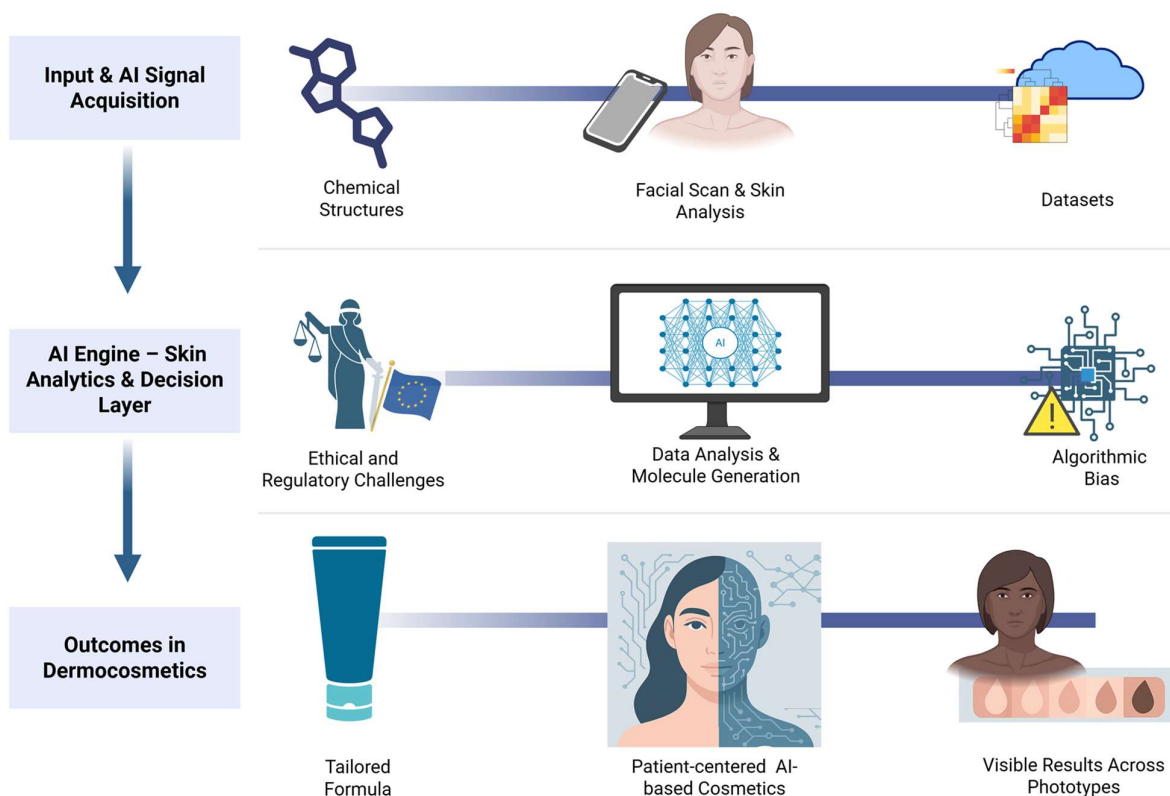


Figure 2. Schematic representation of an AI-driven model for personalized cosmetics formulation. The illustration is structured in three levels: input data acquisition (facial imaging, chemical structures, and

cloud-based health records); analytical and algorithmic processing with emphasis on transparency, regulatory compliance, and bias detection; and output generation, including customized formulations. Created in BioRender. Di Guardo, A. (2025) <https://BioRender.com/l36ic8l>, accessed on 1 July 2025.

5. Conclusions

AI holds the potential to redefine the scientific, ethical, and commercial landscape of cosmetic innovation. Its applications include the production of data-driven formulations through in silico prediction models, optimization of texture and performance and safety testing, as well as compliance with ethical regulations. As such, AI enables more rapid, safe, and sustainable product development, offering tailored solutions that respond to individual needs while respecting societal diversity and environmental constraints. Strong commitment to multidisciplinary collaboration, transparent algorithmic governance, and inclusivity is critical to fully realize this potential. AI is also crucial in the improvement of data quality and in the development of fair, explainable models that prevent bias and foster trust among consumers and regulators. In conclusion, aligning industry practices with emerging regulatory frameworks, investing in robust validation, and ensuring responsible use of consumer data will strengthen AI's role as both a technological enabler and a driver of ethical and sustainable progress in cosmetic science. If implemented responsibly, in fact, AI will not only serve as a powerful innovation tool but also as a catalyst for a more equitable, consumer-centric, and evidence-based future in the cosmetic scenario.

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