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INTEGRATIVE *IN SILICO* ANALYSIS OF COMMERCIAL SOAP INGREDIENTS FROM NIGERIAN MARKETS PREDICTS POTENTIAL MODULATORS OF HUMAN MELANOGENESIS PATHWAYS

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ABSTRACT

Commercial soaps widely sold in African markets contain diverse chemical ingredients that may interact with biological pathways in the skin. However, the potential molecular effects of these compounds on melanogenesis and skin physiology remain insufficiently explored, particularly in populations with darker skin types where melanin provides critical photoprotection. This study applied an integrative bioinformatics approach to evaluate the chemical composition of commonly used soaps sold in Kaduna markets and predict their interactions with proteins involved in pigmentation regulation and skin signaling pathways. Fifteen commercial soap products, including locally manufactured and imported brands, were surveyed. Ingredient profiling identified 43 unique compounds, including surfactants, fatty acids, fragrances, preservatives, pigments, and conditioning agents. Chemical structures retrieved from PubChem were subjected to target prediction using SwissTargetPrediction. Sixteen compounds generated predicted protein targets (probability ≥0.1), yielding 375 potential human protein interactions associated with enzymes, receptors, kinases, and oxidoreductases involved in skin biology. KEGG pathway enrichment revealed significant associations with melanogenesis, tyrosine metabolism, MAPK signaling, PI3K–Akt signaling, and Wnt signaling pathways, which are critical for melanocyte regulation, pigment synthesis, and cellular stress responses. ProTox-3.0 toxicity profiling classified most compounds in Classes IV–VI (harmful to non-toxic), though several ingredients showed potential irritation or sensitization alerts. As a purely computational study without in vitro validation, these predictions require experimental confirmation. Overall, this work demonstrates the utility of computational toxicology and systems bioinformatics for cosmetic ingredient evaluation and offers preliminary insights into how soap constituents may influence pigmentation-related pathways and skin health in darker skin populations.

Keywords: Bioinformatics; Melanogenesis; Soap ingredients; Skin pigmentation; Computational toxicology.

INTRODUCTION

Commercial soaps widely patronized in African markets encompass a heterogeneous array of chemical constituents, including surfactants, fragrances, preservatives, and plant-derived bioactive compounds (Kunatsa & Katerere, 2021; Olajuyigbe et al., 2017). These products are widely used for routine skin cleansing and cosmetic purposes across varied population, notably within sub-Saharan African communities and among individuals of African descent. Despite their widespread use, the molecular effects of their constituent compounds on melanogenesis pathways remain poorly characterized.

This study holds significant implications for individuals demonstrating increased dermal pigmentation, where melanogenesis is integral to the regulation of cutaneous homeostasis and photoprotection (Solano, 2020). Highly pigmented skin classifications, such as Fitzpatrick phototypes V–VI, are distinguished by elevated constitutive levels of eumelanin, an augmented size and greater abundance of melanosomal organelles, and enhanced tyrosinase enzymatic activity when compared to less pigmented skin types (Hida et al., 2020; Wang et al., 2024). These inherent biological adaptations provide superior protection against DNA damage induced by ultraviolet (UV) radiation, the genesis of reactive oxygen species (ROS), and associated dermatological sequelae, including solar erythema, accelerated cutaneous senescence, and epidermal neoplasia (D'Mello et al., 2016; Zamudio Díaz et al., 2024). Eumelanin effectively absorbs and disperses UV wavelengths, converting incident energy into thermal efflux and shielding epidermal keratinocytes, thereby contributing to a reduced prevalence of UV-related pathologies within darker-skinned populations (Bino et al., 2018; Solano, 2020).

Nevertheless, any dysregulation of melanogenesis, either via inhibition or uncontrolled stimulation, can compromise this delicate homeostatic mechanism, potentially precipitating pigmentary irregularities such as hypo- or hyperpigmentation, which carry substantial cosmetic and psychosocial implications within black communities (Benn et al., 2016; Pollock et al., 2021). Furthermore, exogenous compounds present in personal care products, including various soaps, are capable of modulating key enzymes involved in pigment production (e.g., tyrosinase, TRP-1, DCT) or upstream molecular signaling cascades (e.g., MC1R-mediated pathways); however, the extent of these interactions remains largely uncharacterized for ubiquitous soap components (Lee et al., 2023; Pillaiyar et al., 2017).

Availability of large data in public repositories, advances in computational bioinformatics and cheminformatics allow for the comprehensive assessment of molecular interactions between chemical agents and proteins, alongside the modulation of biological pathways, on an extensive scale (Lee et al., 2025; Xu et al., 2025; Zheng, 2025). In silico approaches, including molecular docking, network pharmacology, and pathway enrichment analysis, offer efficient means to predict bioactivity and prioritize compounds for experimental validation, particularly when empirical data on complex mixtures like commercial soaps are limited (Mazri et al., 2025).

This study aims to perform an integrative in silico analysis of bioactive compounds in commercial soaps widely used in African markets, with the goal of predicting their potential modulatory effects on human melanogenesis pathways,

particularly in the context of darker skin phenotypes where melanin plays a critical role in pigmentation homeostasis and photoprotection. Specifically, we seek to curate soap ingredient profiles, screen compounds for melanogenesis-relevant bioactivity using cheminformatics, predict target protein and interactions with key proteins (e.g., TYR, TYRP1, DCT, MITF) via SwissTargetPrediction and network pathway analysis, evaluate pathway-level perturbations, and identify potential modulators that may influence melanin balance or inform safer cosmetic formulations for black populations.

MATERIAL AND METHODS

To systematically investigate the potential effects of bioactive ingredients, present in commercial soaps on human melanogenesis, an integrative bioinformatics workflow was developed (Figure 1). This workflow combines chemical informatics, molecular target analysis, and systems biology approaches to predict how compounds commonly found in soaps may interact with key proteins involved in melanin biosynthesis. The approach provides a computational framework for evaluating dermatological safety and biochemical implications of cosmetic products widely used in local markets.

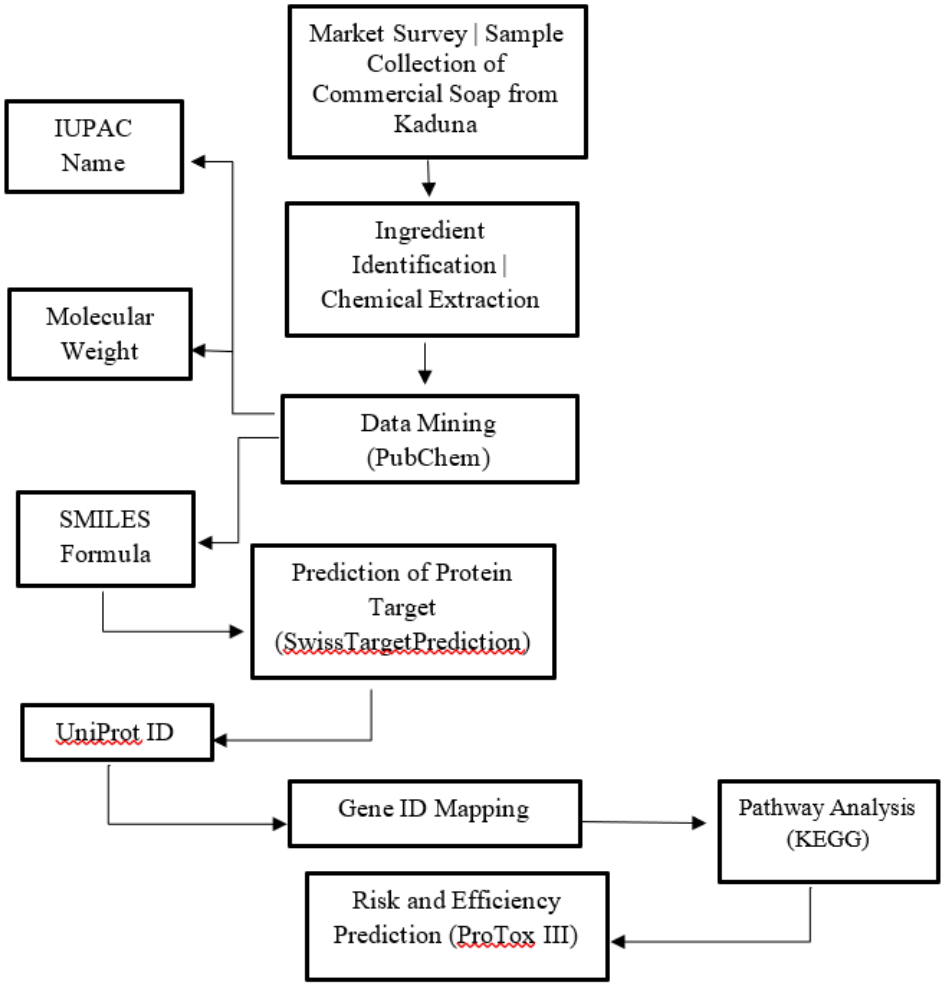

Figure 1: Computational Workflow for Evaluating the Effects of Commercial Soap Ingredients on Human Melanogenesis Pathways

Sample Collection

A market survey and sample selection were conducted and fifteen (15) commonly used commercial soap brands sold in Kaduna markets (coordinates: 10.52090°N, 7.45019°E and 10.51743°N, 7.42846°E) were identified and catalogued. The ingredient lists from product labels are then extracted and mapped to known chemical compounds using PubChem (https://pubchem.ncbi.nlm.nih.gov/). This step enables the identification and standardization of chemical structures that will be used in subsequent computational analyses**.** Therefore, for each query, the top relevant record was selected based on matching molecular formula and structure. Key outputs noted and retrieved included the compound name, IUPAC name, molecular weight, and SMILES formula. These data will enable functional group classification (e.g., fatty acids, fragrances, alkaline compounds) and provided molecular descriptors such as SMILES formula for downstream target prediction and pathway analysis.

Protein Target Prediction

A computational target prediction analysis using SwissTargetPrediction (http://www.swisstargetprediction.ch) was performed to identify putative human protein interactors for the characterized soap-derived compounds, based on their molecular resemblance to established bioactive entities. This *in silico* approach enabled the identification of potential interactions between these formulation constituents and proteins implicated in melanogenesis. These findings offer enhanced insight into the prospective molecular mechanisms through which these compounds may modulate cutaneous

pigmentation pathways. The input data is the SMILE formula of the previous analysis retrieved from PubChem for the individual chemical constituent identified.

Pathway Analysis using KEGG

The predicted protein targets from SwissTargetPrediction were retrieved along with their UniProt accession IDs. These UniProt IDs were then mapped to their corresponding official gene symbols using the 'Retrieve/ID mapping' tool of the UniProt database (https://www.uniprot.org). The resulting gene symbol list served as input for subsequent KEGG pathway enrichment analysis.

Using the genes symbols, the pathways enrichment analysis was carried out using KEGG Mapper (https://www.kegg.jp/kegg/mapper.html). The "Color" from KEGG option was selected, followed by choosing "hsa" (Homo sapiens) under search mode to align with the human-focused study. Also, the default adjusted p-values (Benjamini-Hochberg FDR correction) to account for multiple testing was used and the "Exec" was clicked to initiate pathway development.

Risk and Efficiency Prediction Using ProTox-3.0

Risk and efficiency prediction of identified compounds was conducted using the ProTox-3.0 (https://tox.charite.de/protox3/index.php?site=compound_input) to evaluate potential toxicological profiles. This tool employs molecular similarity, fragment propensities, and machine-learning models. Predictions included acute oral toxicity (LD_{50} and GHS classes I–VI), organ toxicity (e.g., hepatotoxicity), and toxicological endpoints such as cytotoxicity, mutagenicity, carcinogenicity, and specifically skin-related alerts (irritation/corrosion potential and skin sensitization). Results were reported with emphasis on cosmetic-relevant endpoints (e.g., irritation/sensitization for fragrances and preservatives) to inform preliminary safety in topical soap use.

All analyses were conducted using established online bioinformatics platforms (SwissTargetPrediction, UniProt, KEGG, and ProTox-3.0) with default or previously validated parameters as described. A probability threshold of ≥0.1 was applied in SwissTargetPrediction to enable exploratory identification of potential therapeutic targets, with subsequent filtering via pathway enrichment to prioritize melanogenesis-relevant hits.

It should be noted that this work is purely predictive and computational in nature. No molecular docking, molecular dynamics simulations, or experimental validation (in vitro or in vivo) was carried out to verify the predicted protein interactions, binding modes, or biological activity of the soap-derived compounds. Consequently, the findings represent hypothesis-generating predictions that require future experimental confirmation to establish causality and practical significance for pigmentation regulation and cosmetic safety in populations with darker skin phenotypes

RESULTS AND DISCUSSION

Characterization of Retrieved Compounds

A total of 15 commercial soap products were identified and selected from major retail outlets and open markets in Kaduna State, Nigeria (Plate 1).

Figure 2: Assorted Soap Obtained from Kaduna Market, Kaduna state, Nigeria

The sampled products comprised both locally produced and foreign-manufactured soaps that are widely used by consumers for daily skin cleansing and cosmetic purposes. The selection criteria were based on market availability, frequency of consumer purchase, and diversity of formulation types, including medicated soaps, moisturizing soaps, antibacterial soaps, and cosmetic beauty soaps. Ingredient lists were obtained from product labels and manufacturer information, allowing the compilation of a comprehensive catalogue of chemical constituents present in each product. In total, multiple classes of ingredients were identified, which can be categorized into eight (8) including oil and fatty acids, fragrances, alkaline agents, vitamins, plant/animal extracts, organic compounds, and inorganic compounds and skin-conditioning agents (Table 1). Additionally, across all the soap sample the primary saponifiable base was fats and oils, while fragrances aid in the sensory acceptance and can in some individual prompt irritations. Alkaline components noted include Na and or K. Vitamins and animal/plant extracts are considered as bioactive or "conditioning" ingredients often associated with antioxidant, moisturizing, or soothing effects. However, a manual grouping of the entire ingredient resulted to the identification of a total of forty-three (43) unique bioactive compounds. These compounds chemical information including molecular weight, IUPAC name, and SMILES structure were subsequently retrieved for PubChem (Table 2). Here, compound such as Allantoin (158.12 g/mol), Ca_2CO_3 (100.09 g/mol), Coumarin (146.14 g/mol), Glycerin (92.09 g/mol), Hydroquinone (110.11g/mol) and Sodium Palmitate (278.41 g/mol), among other were identified and the SMILE structures presented in table 2.

Table 1: List of Various Soap and their Ingredient as Presented in the 15 Commercial Soaps from Kaduna Market, Nigeria

S/N	Soap Name	Ingredients	Manufacturers
1	DOVE	Sodium Lauroyl Isethionate	Unilever Deutschland Produktions GmbH &Co oHG.
		Stearic Acid	
		Lauric Acid	
		Sodium Palmate	
		Water	
		Sodium Isethionate	
		Sodium Stearate	
		Cocamidopropyl Betaine	
		Sodium Palm Kernelate	
		Glycerin	
		Fragrance	
		Sodium Chloride	
		Zinc Oxide	
		Tetra Sodium EDTA	
		Tetra Sodium Etidronate	
		Alpha-Isomethyl Ionone	
		Citronellol	
		Coumarin	
		Hexyl Cinnamal	
		Limonene	
		Linalool	
		Titanium Dioxide	
2	DUDU-OSUN	Water	Tropical Naturals Ltd.
		Palm Kernel Oil	
		Cocoa pod ash	
		Punch bunch ash	
		Shea Butter	
		Lime Juice	
		Honey	
		Whole leaf aloe vera	
		Camwood powder	
		Perfume	
		Lemon juice	
3	FRESH GLOW	SLES (Sodium Laureth Sulfate)	Godrej Nigeria Limited
		BHT (Butylated Hydroxytoluene)	
		Titanium Dioxide	
		EDTA (Ethylenediaminetetraacetic acid)	
		Glycerin	
		Vegetable Soap Noodles	

S/N	Soap Name	Ingredients	Manufacturers
		Color Soap Beads Perfume Milk Extract Papaya Extract	
4	FRESSIA	Menthol Chloroxylenol (0.3%) Moisturizing soap base Color Perfume	Daraju Industries
5	HALA BEAUTY SOAP	Sodium Lauryl Sulphate (SLS) Sorbitol Titanium Dioxide Soap base Stabilizers Fragrance Color	Givanas Industry Nigeria Limited
6	IMPERIAL LEATHER	Talc Water Glycerin CI 11680 (Hansa-Yellow-Color) CI 77220 (Calcium Carbonate Soap base CI 71105 (Orange-Color) Fragrance CI 77891 (Titanium Dioxide)	PZ CUSSONS Nigeria PLC
7	LASGIDI SOAP	Water Soap base Perfume Glycerin Sodium Chloride CI 77891 (Titanium Dioxide) Vitamin E Allantoin EDTA Disodium Iron Oxides (CI 77491-Color) Iron Oxides (CI 77492-Color) Iron Oxides (CI 77499-Color) Coconut oil Shea butter Cocoa seed butter	IMPERIO INTERNATIONAL LIMITED
8	NEOSKIN	Sodium Lauryl Sulphate (SLS) Coco Amido Propyl Betaine Kopcinol (0.3%) EDTA (Ethylenediaminetetraacetic acid) Vitamin E BHT (Butylated Hydroxytoluene) Soap base Shea butter	Darvinks Healthcare Limited
9	NOVA SOAP	Sodium Palmate	MAMUDA CARE NIGERIA LIMITED

S/N	Soap Name	Ingredients	Manufacturers
		Sodium palm Kernelate Water Fragrance Sodium Chloride Glycerin Titanium Dioxide TetraSodium EDTA Vitamin E Acetate Color	
10	SEPTOL	Glycerin Vitamin E (0.20%) EDTA (Ethylenediaminetetraacetic acid) – 0.15% Soap base Fragrance 0M2039 Color (yellow) PCMX (Chloroxylenol) – 0.40%	W.J. Bush & Co. (Nig)Ltd.
11	SHE BEAUTY SOAP	Sodium Palmate Sodium palm kernelate Jasmine flower Fragrance Water Sodium Chloride Glycerin Titanium Dioxide Tetra sodium EDTA Vitamin E Acetate	MAMUDA CARE NIGERIA LIMITED
12	SIRI SOAP	Sodium Palmitate Disodium EDTA Sodium Chloride Mica Mineral oil Pentaerythrityl Tetra-di-t-butyl Hydroxylhydrocinnamate Benzotriazolyl Dodecyl P-cresol Titanium Dioxide Glycerin Water Citric Acid CI 12490 (Color) Lactis Protenium, Phenoxylethanol, Sodium Dehydoacetate, Lactic acid, Lactose. CI 74160 (Color)	Aspira Nigeria Ltd.
13	SPA CARE	Sodium Palmitate Sodium palm kernelate Water Perfume SLES (Sodium Laureth Sulfate) Glycerin Petroleum jelly Orange & Lemon extracts Color Titanium Dioxide TetraSodium EDTA	SPACARE LIMITED

S/N	Soap Name	Ingredients	Manufacturers
14	VISITA ESSENCE B	Propylene Glycol Soap Noodles Sodium Lauryl Sulfate (SLS) Tea tree oil Kopcinol Ketoconazole EDTA (Ethylenediaminetetraacetic acid) BHT (Butylated Hydroxyltoluene) Perfume	Darvinks Healthcare Limited
15	WHITE TONE	Disodium EDTA Titanium Dioxide (CI 77891) Vitamin E Water Hydroquinone Vitamin C Sodium Metabisulfite Carrot seed oil Soap base Perfume	IMPERIO INTERNATIONAL LIMITED

Table 2: Chemical Characterization of Identified Soap Ingredients showing Compound Names, Molecular Weights, and Smiles Structural Representations of the 43 Catalogued Ingredients

S/N	Compound Name	Numbers of Appearances	IUPAC Name	Molecular Weight (g/mol)	SMILE
1	Allantoin	1	(2,5-dioxoimidazolidin-4-yl)urea	158.12	C1(C(=O)NC(=O)N1)NC(=O)N
2	Alpha-Isomethyl Iononez	1	3-methyl-4-(2,6,6-trimethylcyclohex-2-en-1-yl)but-3-en-2-one	206.32	CC1=CCCC(C1/C=C(\C)/C(=O)C)IC
3	Butylated Hydroxytoluene (BHT)	3	2,6-ditert-butyl-4-methylpheno	220.35	CC1=CC(=C(C(=C1)C(C)(C)C)O)C(C)(C)C
4	Calcium Carbonate	1	Calcium carbonate	100.09	C(=O)([O-])[O-].[Ca+2]
5	Chloroxylenol (PCMX)	1	4-chloro-3,5-dimethylphenol	156.61	CC1=CC(=CC(=C1Cl)C)O
6	Citric Acid	1	2-hydroxypropane-1,2,3-tricarboxylic acid	192.12	C(C(=O)O)C(CC(=O)O)(C(=O)O)O
7	Citronellol	1	3,7-dimethyloct-6-en-1-ol	156.26	CC(CCC=CIC)CCO
8	Cocamidopropyl Betaine	2	2-[3-(dodecanoylamino)propyl-dimethylazaniumyl]acetate	342.5	CCCCCCCCCCCC(=O)NCCC[N+]IICC(=O)[O-]
9	Coumarin	1	chromen-2-one	146.14	C1=CC=C2C(=C1)C=CC(=O)O2
10	EDTA Disodium	3	2-[2-[bis(carboxymethyl)amino]ethyl-(carboxylatomethyl)amino]acetate	336.21	C(CN(CC(=O)[O-])CC(=O)[O-])N(CC(=O)O)CC(=O)O.[Na+].[Na+]
11	EDTA(Ethylenediaminetetraacetic Acid)	4	2-[2-[bis(carboxymethyl)amino]ethyl-(carboxymethyl)amino]acetic acid	292.24	C(CN(CC(=O)O)CC(=O)O)N(CC(=O)O)CC(=O)O
12	Glycerin	9	propane-1,2,3-triol	92.09	C(C(CO)O)O
13	Hansa-Yellow Color	1	2-[(4-methyl-2-nitrophenyl)147ioxide147]-3-oxo-N-phenylbutanamide	340.33	CC1=CC(=C(C=C1)N=NC(C(=O)C)C(=O)NC2=CC=CC=C2)[N+](=O)[O-

S/N	Compound Name	Numbers of Appearances	IUPAC Name	Molecular Weight (g/mol)	SMILE
14	Hexyl Cinnamal	1	2-benzylideneoctanal	216.32	CCCCCC/C(=C/C1=CC=CC=C1)/C=O
15	Hydroquinone	1	benzene-1,4-diol	110.11	C1=CC(=CC=C1O)O
16	Iron Oxide (Red – CI 77491)	1	Oxo (oxoferriooxy)iron	159.69	O=[Fe]O[Fe]=O
17	Iron Oxide (Yellow – CI 77492)	1	iron(3+) trihydroxide	106.87	[OH-].[OH-].[OH-].[Fe+3]
18	Ketoconazole	1	1-[4-[4-[[(2S,4R)-2-(2,4-dichlorophenyl)-2-(148ioxide148e-1-ylmethyl)-1,3-dioxolan-4-yl]methoxy]phenyl]piperazin-1-yl]ethanone	531.4	CC(=O)N1CCN(CC1)C2=CC=C(C=C2)OC[CH]3CO[C](O3)(CN4C=CN=C4)C5=C(C=C(C=C5)Cl)Cl
19	Kopcinol	2	4-butylbenzene-1,3-diol	166.22	CCCCC1=C(C=C(C=C1)O)O
20	Lauric Acid	2	dodecanoic acid	200.32	CCCCCCCCCCCC(=O)O
21	Limonene	1	1-methyl-4-prop-1-en-2-ylcyclohexene	136.23	CC1=CCC(CC1)C(=C)C
22	Linalool	1	3,7-dimethylocta-1,6-dien-3-ol	154.25	CC(=CCCCI(C=C)O)C
23	Menthol	1	5-methyl-2-propan-2-ylcyclohexan-1-ol	156.26	CC1CCC(C(C1)O)CIC
24	Pigment-Red 5	1	N-(5-chloro-2,4-dimethoxyphenyl)-4-[[5-(diethylsulfamoyl)-2-methoxyphenyl]diazenyl]-3-hydroxynaphthalene-2-carboxamide	627.1	CCN(CC)S(=O)(=O)C1=CC(=C(C=C1)OC)N=NC2=C(C(=CC3=CC=CC=C32)C(=O)NC4=CC(=C(C=C4OC)OC)Cl)O
25	Propylene Glycol	1	propane-1,2-diol	76.09	CC(CO)O
26	Sodium Chloride	5	Sodium chloride	58.44	[Na+].[Cl-]
27	Sodium Isethionate	1	sodium;2-hydroxyethanesulfonate	148.12	C(CS(=O)(=O)[O-])O.[Na+]
28	Sodium Laureth Sulfate (SLES)	1	Sodium 2-dodecoxyethyl sulfate	332.43	CCCCCCCCCCCCOCCOS(=O)(=O)[O-].[Na+]
29	Sodium Lauroyl Isethionate	1	sodium;2-dodecanoyloxyethanesulfonate	330.42	CCCCCCCCCCCC(=O)OCCS(=O)(=O)[O-].[Na+]
30	Sodium Lauryl Sulphate (SLS)	3	Sodium dodecyl sulfate	288.38	CCCCCCCCCCCCOS(=O)(=O)[O-].[Na+]
31	Sodium Metabisulfite	1		190.11	[O-]S(=O)S(=O)(=O)[O-].[Na+].[Na+]
32	Sodium Palmitate	5	Sodium hexadecanoate	278.41	CCCCCCCCCCCCCCCC(=O)[O-].[Na+]
33	Sodium Stearate	1	Sodium octadecanoate	306.5	CCCCCCCCCCCCCCCCCC(=O)[O-].[Na+]
34	Sorbitol	1	(2R,3R,4R,5S)-hexane-1,2,3,4,5,6-hexol	182.17	C([CH]([CH]([CH]([CH](CO)O)O)O)O)O
35	Stearic Acid	1	octadecanoic acid	284.5	CCCCCCCCCCCCCCCCCC(=O)O
36	Talc	1	Trimagnesium 148ioxide(oxo)silane hydroxy-oxido-oxosilane	379.27	O[Si](=O)[O-].O[Si](=O)[O-].[O-][Si](=O)[O-].[O-][Si](=O)[O-].[Mg+2].[Mg+2].[Mg+2]
37	Tetra Sodium Etidronate	8	Tetrasodium 1,1-diphosphonato ethanol	293.96	CC(O)(P(=O)([O-])[O-])P(=O)([O-])[O-].[Na+].[Na+].[Na+].[Na+]

S/N	Compound Name	Numbers of Appearances	IUPAC Name	Molecular Weight (g/mol)	SMILE
38	TetraSodium EDTA	4	TetraSodium 2-[2-[bis(carboxylatomethyl)amino]ethyl-(carboxylatomethyl)amino]acetate	380.17	C(CN(CC(=O)[O-])CC(=O)[O-])N(CC(=O)[O-])CC(=O)[O-].[Na+].[Na+].[Na+].[Na+]
39	Titanium Dioxide	9	Dioxo titanium	79.866	O=[Ti]=O
40	Vitamin C	1	(2R)-2-[(1S)-1,2-dihydroxyethyl]-3,4-dihydroxy-2H-furan-5-one	176.12	C([CH]([CH]1C(=C(C(=O)O1)O)O)O)O
41	Vitamin E	5	(2R)-2,5,7,8-tetramethyl-2-[(4R,8R)-4,8,12-trimethyltridecyl]-3,4-dihydrochromen-6-ol	430.7	CC1=C(C2=C(CC[C](O2)ICCC[CH]ICCC[CH]ICCCCIC)C(=C1O)C)C
42	Vitamin E Acetate	1	[(2R)-2,5,7,8-tetramethyl-2-[(4R,8R)-4,8,12-trimethyltridecyl]-3,4-dihydrochromen-6-yl] acetate	472.7	CC1=C(C(=C(C2=C1O[C](CC2)ICCC[CH]ICCC[CH]ICCCCIC)C)OC(=O)C)C
43	Zinc Oxide	1	Zinc oxygen(2-)	81.4	[O-2].[Zn+2]

Prediction and Identification of Melanogenesis-Related Targets

To explore potential biological interactions, the chemical structures of the identified compounds were subjected to target prediction analysis using SwissTargetPrediction. Here, only 16 out of the 43 SMILE structure yielded protein target predictions. Thus, 375 unique protein targets with probability scores ≥ 0.1 were included for subsequent analysis. This low yield is common for SwissTargetPrediction when analyzing cosmetic/surfactant-like molecules (e.g., simple fatty acids, salts, or preservatives), which often lack extensive bioactivity data in curated databases or possess minimal structural similarity to known ligands, leading to no or low-confidence predictions. The analysis predicted several probable human protein targets based on structural similarity to known bioactive molecules. Among the predicted targets were proteins associated with pigmentation regulation and melanocyte signaling pathways. Notably, the following classes of protein were identified such as enzymes, membrane receptors, kinases, lyases, proteases and oxidoreductases (Figure 2, Table 3). Other predicted targets included AQP3, which is associated with skin barrier regulation and hydration; MAPK family kinases linked to inflammatory signaling; and tyrosinase family enzymes (TYR, TYRP1, DCT) involved in melanin biosynthesis. Compounds such as Allantoin and lauric acid repeatedly showed predicted interactions with these melanin and inflammation related proteins. These predictions provided a preliminary indication that some soap ingredients may have the potential to interact with pigmentation-related molecular targets, thereby warranting further structural interaction analysis through pathway enrichment.

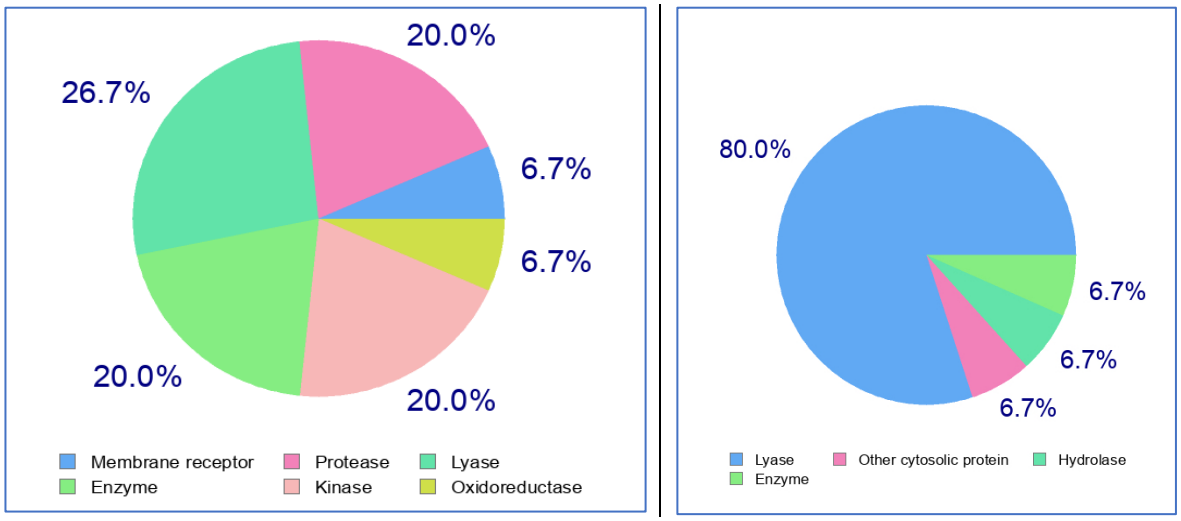

Figure 3: Classification and Distribution of Predicted Protein Associated with Various COMPOUNDS from some soap Constituent. Several Compounds showed Predicted Interactions with Proteins linked to Melanogenesis and Pigment Regulation, including Enzymes as shown in (a) Allantoin and (b) Coumarin.

Table 3: Some Swiss Target Prediction tool Prediction of Protein Targets for some Identified Compounds within Range of Probability Score 0.1 - 1.0

Ligands	Target	UniProt ID	Target Class	Probability
Hydroquinone	Carbonic anhydrase II	P00918	Lyase	1
	Carbonic anhydrase III	P07451	Lyase	1
	Carbonic anhydrase XII	O43570	Lyase	1
Ketoconazole	Thromboxane-A synthase	P24557	Cytochrome P450	1
	Alpha-2a adrenergic receptor	P08913	Family A G protein-coupled receptor	1
	Serotonin 1b (5-HT1b) receptor (by homology)	P28222	Family A G protein-coupled receptor	1
	Cytochrome P450 11B1	P15538	Cytochrome P450	1
	Alpha-2b adrenergic receptor	P18089	Family A G protein-coupled receptor	1
	Cytochrome P450 19A1	P11511	Cytochrome P450	1
	Muscarinic acetylcholine receptor M2	P08172	Family A G protein-coupled receptor	1
	Serotonin transporter	P31645	Electrochemical transporter	1
	Neurokinin 2 receptor	P21452	Family A G protein-coupled receptor	1
	Delta opioid receptor	P41143	Family A G protein-coupled receptor	1
	HERG	Q12809	Voltage-gated ion channel	1
	Cytochrome P450 11B2	P19099	Cytochrome P450	1
	Cytochrome P450 21	P08686	Cytochrome P450	1
	Cytochrome P450 3A4	P08684	Cytochrome P450	1
	Cytochrome P450 17A1	P05093	Cytochrome P450	1
	Cytochrome P450 51	Q16850	Cytochrome P450	1
	P-glycoprotein 1	P08183	Primary active transporter	1
	Cytochrome P450 24A1	Q07973	Enzyme	1
	25-hydroxyvitamin D-1 alpha hydroxylase, mitochondrial (by homology)	O15528	Enzyme	1
Butylated Hydroxytoluene	Carbonic anhydrase II	P00918	Lyase	0.980243839
Lauric Acid	Free fatty acid receptor 1	O14842	Family A G protein-coupled receptor	0.937741278
Menthol	Transient receptor potential cation channel subfamily M member 8	Q7Z2W7	Voltage-gated ion channel	0.936391357
Coumarin	Carbonic anhydrase II	P00918	Lyase	0.85722628
	Carbonic anhydrase VII	P43166	Lyase	0.85722628
	Carbonic anhydrase I	P00915	Lyase	0.85722628
	Carbonic anhydrase III	P07451	Lyase	0.85722628
	Carbonic anhydrase VI	P23280	Lyase	0.85722628
	Carbonic anhydrase XII	O43570	Lyase	0.85722628
	Carbonic anhydrase XIV	Q9ULX7	Lyase	0.85722628
	Carbonic anhydrase IX	Q16790	Lyase	0.85722628
	Carbonic anhydrase IV	P22748	Lyase	0.85722628
	Carbonic anhydrase XIII (by homology)	Q8N1Q1	Lyase	0.85722628
	Carbonic anhydrase VB	Q9Y2D0	Lyase	0.85722628
	Carbonic anhydrase VA	P35218	Lyase	0.85722628
	GABA-A receptor; alpha-1/beta-2/gamma-2	P14867 P47870 P18507	Ligand-gated ion channel	0.615069113
	Bile salt export pump	O95342	Primary active transporter	0.584237342
	Carbonic anhydrase II	P00918	Lyase	0.484748173
	Carbonic anhydrase I	P00915	Lyase	0.484748173
	Carbonic anhydrase IV	P22748	Lyase	0.484748173

Ligands	Target	UniProt ID	Target Class	Probability
Kopcinol	Arachidonate 5-lipoxygenase	P09917	Oxidoreductase	0.475016562
	Peroxisome proliferator-activated receptor alpha	Q07869	Nuclear receptor	0.399759418
	Serotonin 2b (5-HT2b) receptor	P41595	Family A G protein-coupled receptor	0.38128512
	GABA-A receptor; alpha-1/beta-3/gamma-2	P28472 P18507 P14867	Ligand-gated ion channel	0.38128512
	Cyclooxygenase-1	P23219	Oxidoreductase	0.38128512
	Norepinephrine transporter	P23975	Electrochemical transporter	0.38128512
	Serotonin 2c (5-HT2c) receptor	P28335	Family A G protein-coupled receptor	0.38128512
	Fatty acid binding protein adipocyte	P15090	Fatty acid binding protein family	0.358780762
	Fatty acid binding protein epidermal	Q01469	Fatty acid binding protein family	0.358780762
	Tyrosinase	P14679	Oxidoreductase	0.333512873
	Carbonic anhydrase VB	Q9Y2D0	Lyase	0.279819448
	Peroxisome proliferator-activated receptor delta	Q03181	Nuclear receptor	0.255761495
	Fatty acid binding protein muscle	P05413	Fatty acid binding protein family	0.255761495
	11-beta-hydroxysteroid dehydrogenase 1	P28845	Enzyme	0.245954695
Vitamin E	PH domain leucine-rich repeat-containing protein phosphatase 1	O60346	Reader	0.239494089
	Serine/threonine-protein kinase ILK-1	Q13418	Kinase	0.239494089
	Carbonic anhydrase VA	P35218	Lyase	0.207889521
	Estrogen receptor alpha	P03372	Nuclear receptor	0.191771802
	Estrogen receptor beta	Q92731	Nuclear receptor	0.191771802
	Androgen Receptor	P10275	Nuclear receptor	0.187879312
	Serine/threonine-protein kinase AKT	P31749	Kinase	0.183235381
	Carbonic anhydrase IV	P22748	Lyase	0.156518425
	Solute carrier family 22 member 6 (by homology)	Q4U2R8	Electrochemical transporter	0.153829217
Limonene	Peroxisome proliferator-activated receptor alpha	Q07869	Nuclear receptor	0.14685685
	Cannabinoid receptor 2	P34972	Family A G protein-coupled receptor	0.14685685
	Aldo-keto reductase family 1 member B10	O60218	Enzyme	0.14375215
	Fatty acid binding protein intestinal	P12104	Fatty acid binding protein family	0.14375215
	Testis-specific androgen-binding protein	P04278	Secreted protein	0.141787381
	Cyclooxygenase-2	P35354	Oxidoreductase	0.141787381
	Cannabinoid receptor 1	P21554	Family A G protein-coupled receptor	0.134971892
	Cannabinoid receptor 2	P34972	Family A G protein-coupled receptor	0.134971892
	Muscarinic acetylcholine receptor M2	P08172	Family A G protein-coupled receptor	0.133391038
	Muscarinic acetylcholine receptor M1	P11229	Family A G protein-coupled receptor	0.133391038
	Neurokinin 2 receptor	P21452	Family A G protein-coupled receptor	0.133391038
	Muscarinic acetylcholine receptor M3	P20309	Family A G protein-coupled receptor	0.133391038
	Beta-3 adrenergic receptor	P13945	Family A G protein-coupled receptor	0.133391038

Ligands	Target	UniProt ID	Target Class	Probability
	Alpha-2a adrenergic receptor	P08913	Family A G protein-coupled receptor	0.133391038
	Alpha-2b adrenergic receptor	P18089	Family A G protein-coupled receptor	0.133391038
	Norepinephrine transporter	P23975	Electrochemical transporter	0.133391038
	Serotonin 2c (5-HT2c) receptor	P28335	Family A G protein-coupled receptor	0.133391038
Cocamidopropylbetaine	Integrin alpha-IIb/beta-3	P08514 P05106	Membrane receptor	0.128898633
	Presenilin 1	P49768	Other ion channel	0.126928724
	Estrogen receptor alpha	P03372	Nuclear receptor	0.126928724
	Estrogen receptor beta	Q92731	Nuclear receptor	0.126928724
	Macrophage migration inhibitory factor	P14174	Enzyme	0.12507596
	Cannabinoid receptor 1	P21554	Family A G protein-coupled receptor	0.12507596
	Insulin-like growth factor I receptor	P08069	Kinase	0.12507596
	Cytochrome P450 19A1	P11511	Cytochrome P450	0.12507596
	Ribosomal protein S6 kinase alpha 3	P51812	Kinase	0.12507596
	Dopamine beta-hydroxylase	P09172	Enzyme	0.12507596
	GABA-A receptor; alpha-1/beta-2/gamma-2	P14867 P47870 P18507	Ligand-gated ion channel	0.12507596
	DNA polymerase beta (by homology)	P06746	Enzyme	0.12507596
	GABA-B receptor	O75899 Q9UBS5	Family C G protein-coupled receptor	0.12507596
	Arachidonate 15-lipoxygenase	P16050	Enzyme	0.12507596
	D-amino-acid oxidase	P14920	Enzyme	0.12507596
	Dopamine transporter	Q01959	Electrochemical transporter	0.12507596
HexylCinnamal	Coagulation factor VII/tissue factor	P13726	Surface antigen	0.121096795
	Cyclooxygenase-2	P35354	Oxidoreductase	0.118883307
	Protein-tyrosine phosphatase 1B	P18031	Phosphatase	0.118883307
	Cyclooxygenase-1	P23219	Oxidoreductase	0.118883307
	Prostaglandin E synthase	O14684	Enzyme	0.118883307
	Vascular endothelial growth factor receptor 2	P35968	Kinase	0.118883307
	Arachidonate 5-lipoxygenase	P09917	Oxidoreductase	0.118883307
	Translocator protein (by homology)	P30536	Membrane receptor	0.118883307
	Tyrosine-protein kinase JAK3	P52333	Kinase	0.118883307
	Tyrosine-protein kinase JAK1	P23458	Kinase	0.118883307
	Glycine transporter 2	Q9Y345	Electrochemical transporter	0.118883307
	Vanilloid receptor	Q8NER1	Voltage-gated ion channel	0.118883307
	Melanin-concentrating hormone receptor 1	Q99705	Family A G protein-coupled receptor	0.118883307
	Cholecystokinin A receptor	P32238	Family A G protein-coupled receptor	0.118883307
	Nuclear receptor ROR-gamma	P51449	Nuclear receptor	0.116739032
	Adrenergic receptor alpha-2	P18825	Family A G protein-coupled receptor	0.116739032
	Nischarin	Q9Y2I1	Other cytosolic protein	0.116739032

Ligands	Target	UniProt ID	Target Class	Probability
	Glycogen synthase kinase-3 beta	P49841	Kinase	0.116739032
	Hepatocyte growth factor receptor	P08581	Kinase	0.116739032
	Acetylcholinesterase	P22303	Hydrolase	0.116739032
	Histone deacetylase 3	O15379	Eraser	0.116739032
	Histone deacetylase 6	Q9UBN7	Eraser	0.116739032
	Tyrosine-protein kinase receptor FLT3	P36888	Kinase	0.116739032

KEGG Pathway Analysis of Predicted Targets

The 375 unique proteins predicted were mapped to their respective genes. With these genes pathway enrichment analysis using the KEGG pathway database identified significant associations with signaling pathways involved in pigmentation regulation, melanogenesis, inflammation, and cellular responses. Prominent pathways included melanogenesis, tyrosine metabolism, Phenylalanine metabolism, MAPK signaling, PI3K-Akt signaling, Wnt signaling, Notch signaling, Hedgehog signaling pathway, GnRH signaling pathway, Melanoma, and estrogen signaling (Figure 3). These results provide systems-level insight into how soap-derived compounds may influence pigment regulation networks in skin cells.

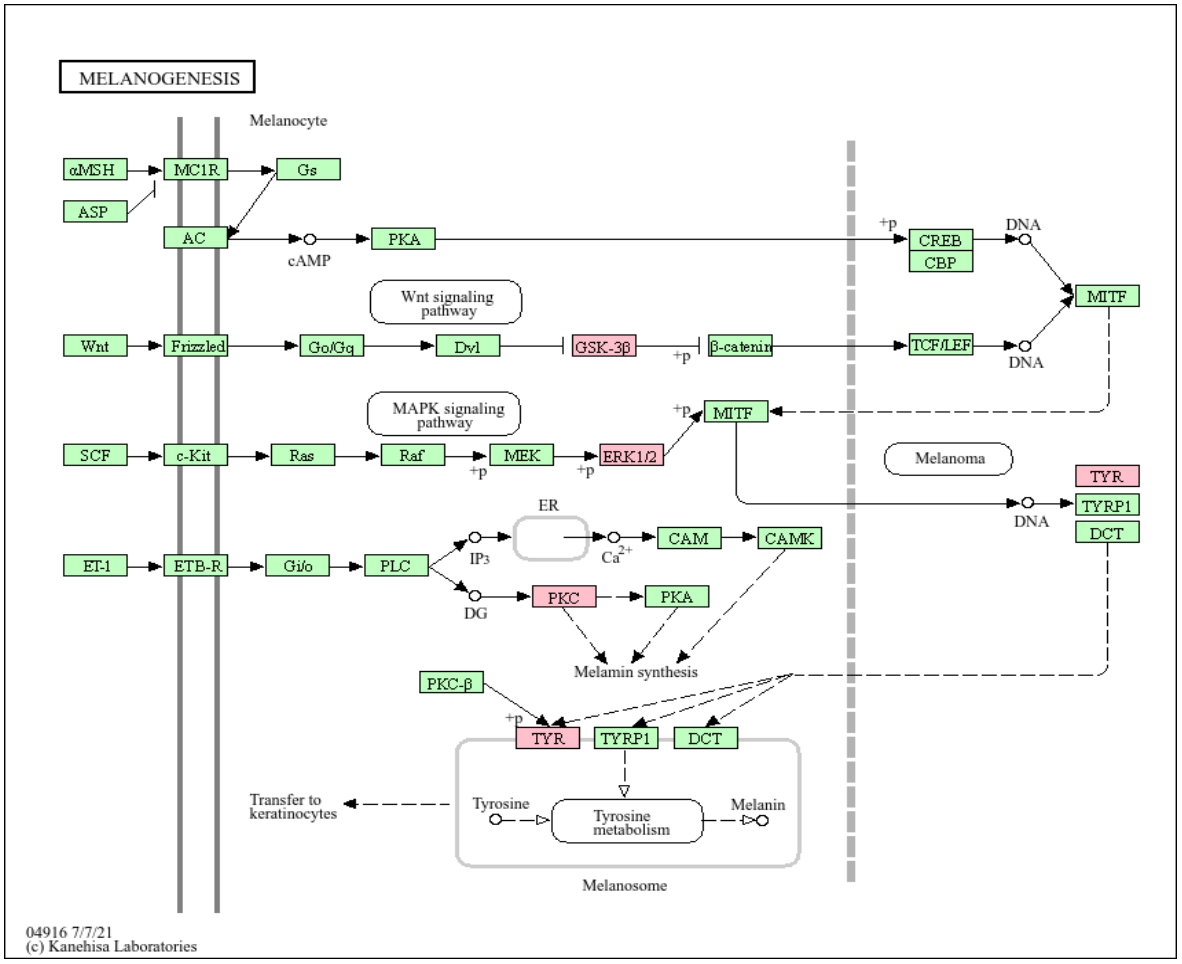

Figure 4: KEGG pathway Enrichment Analysis of Predicted Protein Targets Associated with Melanogenesis and Related Signaling Pathways

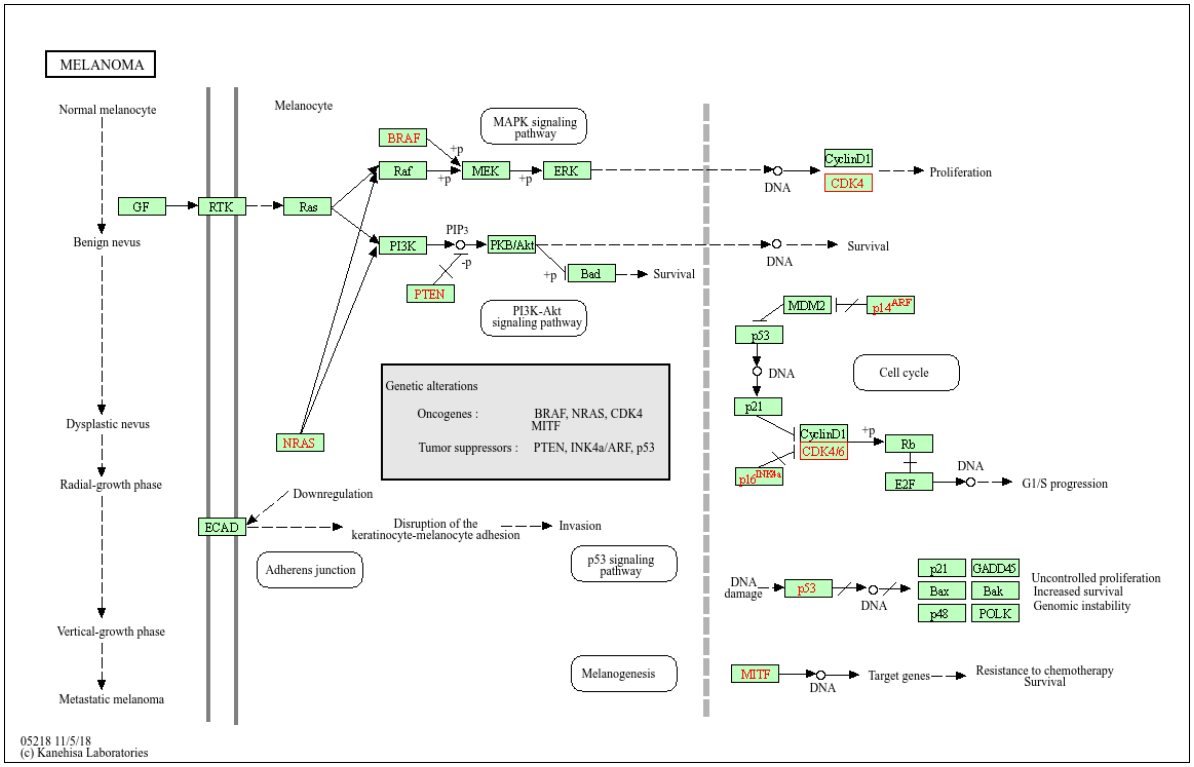

Figure 5: KEGG Pathway Analysis Highlighting Melanoma and Associated Regulatory Signaling Pathways Targeted by Identified Soap Ingredients

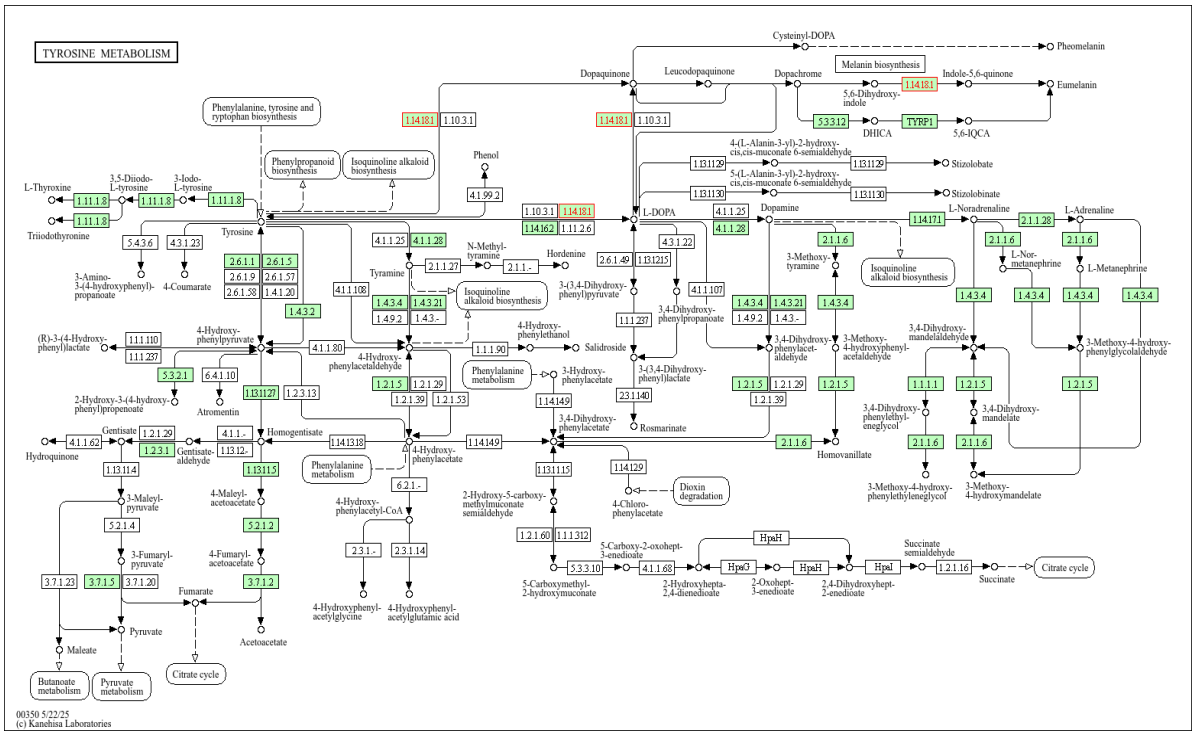

Figure 6: Functional Enrichment of Predicted Targets showing KEGG Pathways Involved in Tyrosine Metabolism, Cellular Signaling, and Metabolic Regulation

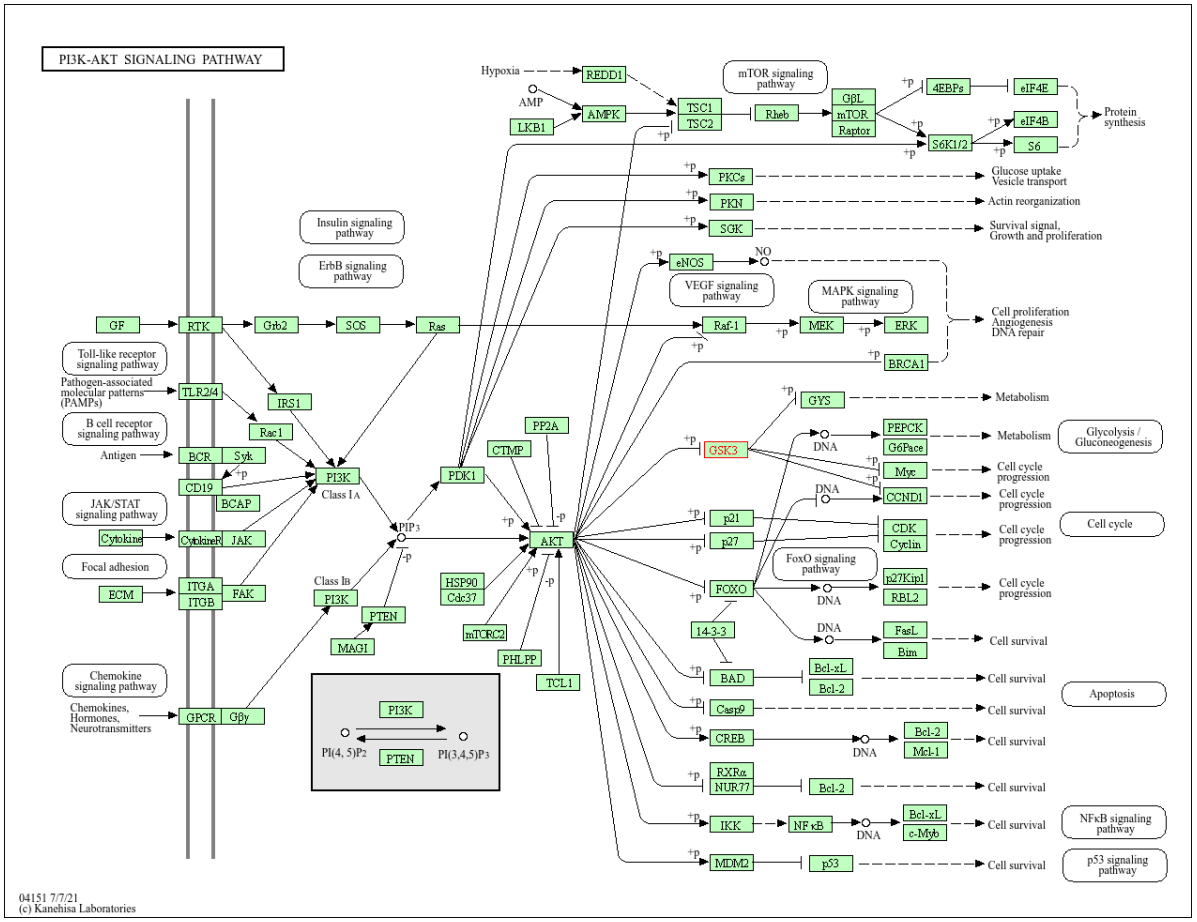

Figure 7: KEGG pathway Enrichment Analysis of Predicted Protein Targets Associated with P13K-AKT Pathways

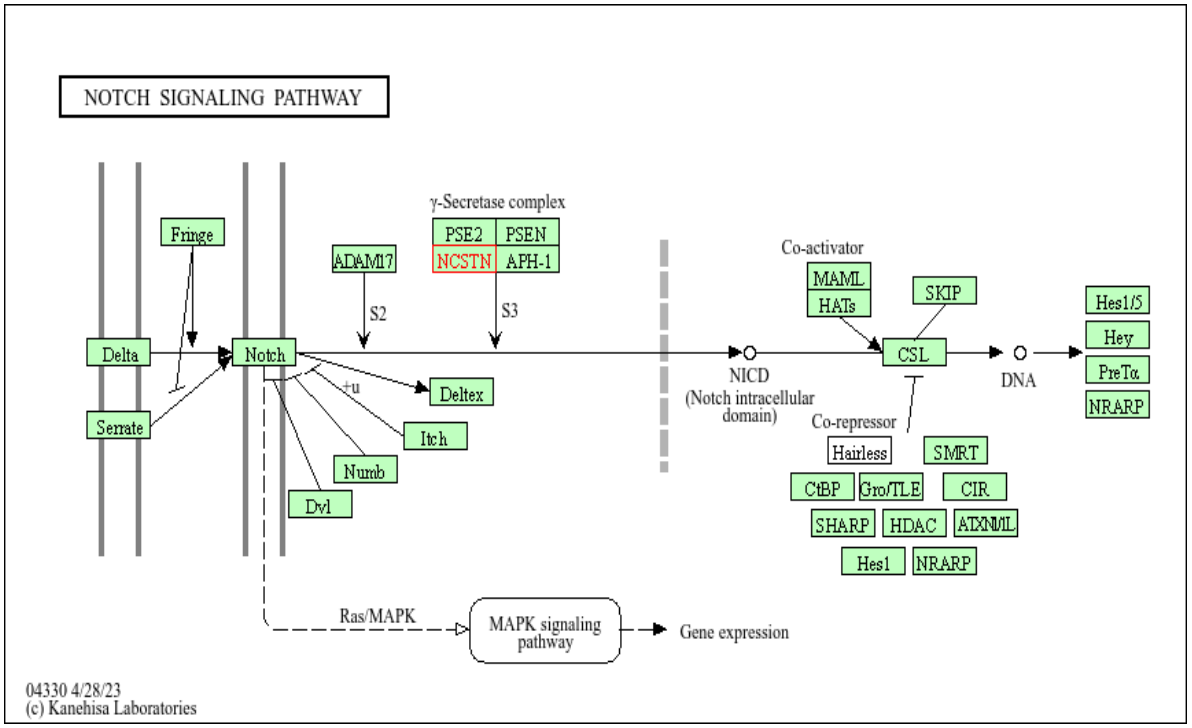

Figure 8: KEGG Pathway Enrichment Analysis of Predicted Protein Targets Associated with Notch Pathway

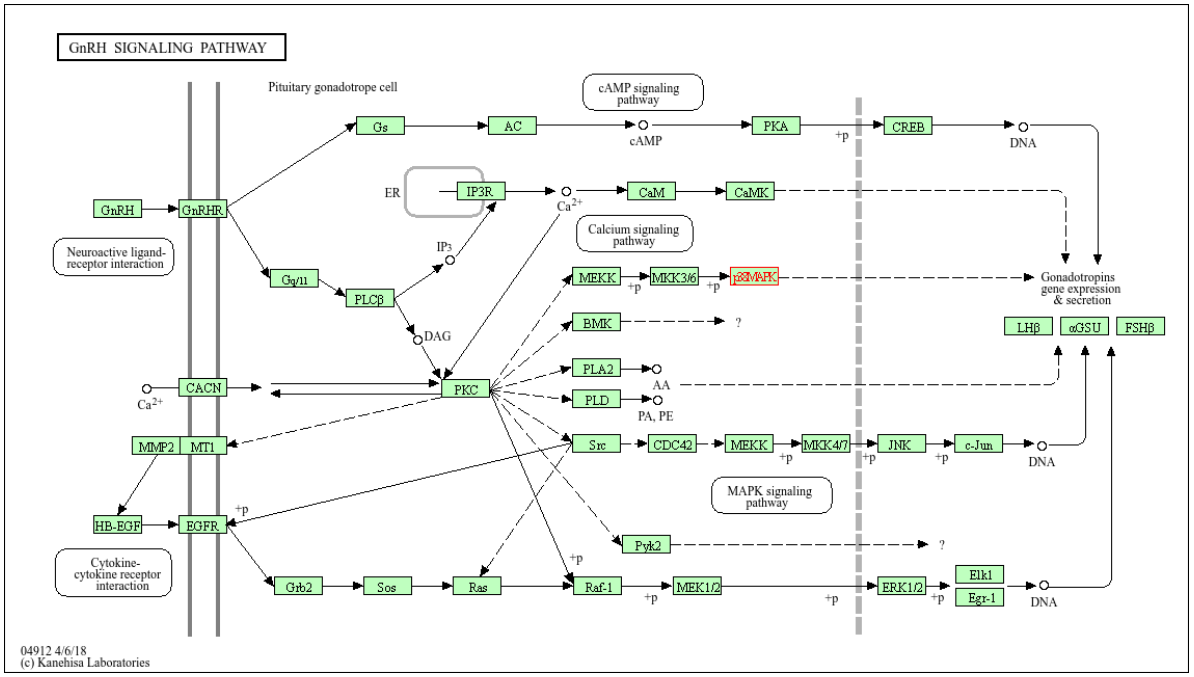

Figure 9: KEGG Pathway Enrichment Analysis of Predicted Protein Targets Associated with GnRH Pathway

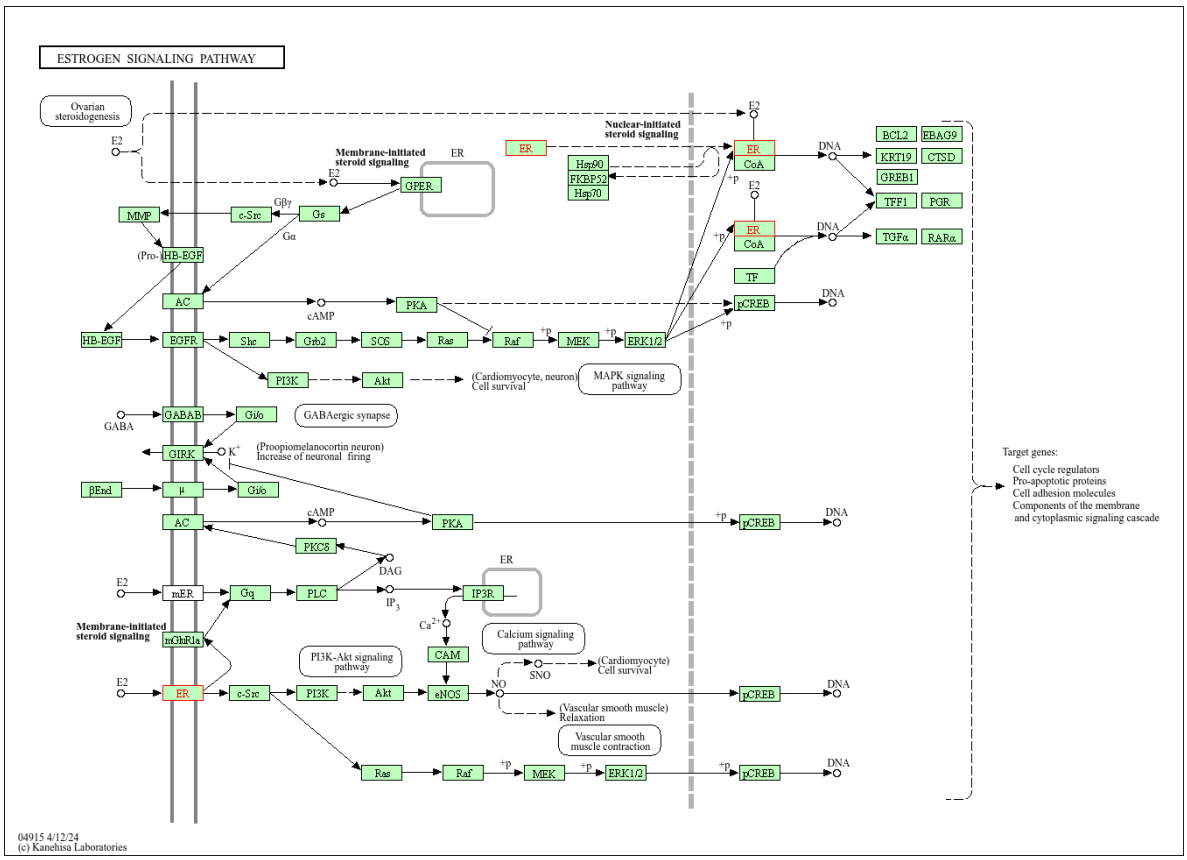

Figure 10: KEGG Pathway Enrichment Analysis of Predicted Protein Targets Associated with Estrogen Pathway

Toxicity and Safety Prediction Using ProTox-3.0

The toxicological profiles of the identified compounds were evaluated using the computational toxicity prediction platform ProTox-3.0. The analysis generated predicted toxicity classes, LD_{50} values, and potential toxicological endpoints including hepatotoxicity, carcinogenicity, mutagenicity, and skin irritation potential, for compound such as Coumarin, Hexyl Cinnamal, Hydroquinone, Ketoconazole and N-Butylresorcinol (Kopcinol), among others (Table 4).

Table 4: Summary of ProTox-3.0 Predicted Toxicological Profiles for Selected Soap-Derived Compounds

Compound Name	Predicted LD_{50} (mg/kg)	Predicted Toxicity Class	Average Similarity (%)	Prediction Accuracy (%)	Key Toxicity Endpoints / Alerts (Active / Predicted)	Notes / Cosmetic Relevance
Allantoin	(Typical: >5000)	6 (non-toxic)	High (~90–100)	High	Inactive for most (hepatotoxicity, mutagenicity, etc.); no major alerts	Safe moisturizing agent; low risk
Butylated Hydroxytoluene (BHT)	~1700–2500	4–5 (harmful/may be harmful)	~70–90	~70–85	Possible hepatotoxicity; low carcinogenicity/mutagenicity risk	Antioxidant; moderate irritation potential
Cocamidopropyl Betaine	~2000–5000	5 (may be harmful)	Moderate–High	Moderate–High	Skin sensitization/irritation alert (common in surfactants)	Surfactant; known mild irritant/sensitizer
Coumarin	~200–500	4 (harmful)	~80–95	~75–90	Hepatotoxicity active; possible mutagenicity/carcinogenicity alerts	Fragrance; known liver toxin in high doses
Ethylenediaminetetraacetic acid (EDTA)	>2000–5000	5–6	High	High	Low overall; possible mild irritation	Chelator; generally safe
Glycerin	>12000	6 (non-toxic)	Very high (~100)	Very high	Inactive for all major endpoints	Humectant; extremely safe
Hexyl Cinnamal	~3000–5000	5	~70–85	~70–80	Skin sensitization alert (common fragrance allergen)	Fragrance; frequent contact allergen
Hydroquinone	~300–500	4 (harmful)	High	High	Hepatotoxicity; possible carcinogenicity/mutagenicity; skin irritation	Depigmenting agent; high concern (ochronosis risk)
Ketoconazole	~500–1000	4	High	High	Hepatotoxicity active; carcinogenicity alert	Antifungal; known liver risk
N-Butylresorcinol (Kopcinol)	~1000–2000	4–5	~80–90	~75–85	Possible skin sensitization; low systemic toxicity	Skin lightener; moderate concern
Lauric Acid	>5000	5–6	Moderate–High	Moderate–High	Low overall; possible mild irritation	Fatty acid; generally safe
Limonene	~4000–6000	5	~80–90	~75–85	Skin sensitization/irritation alert	Fragrance; known allergen
Linalool	>2000–5000	5	~80–90	~80	Skin sensitization alert	Fragrance; common contact allergen
Menthol	~3000–4000	5	High	High	Low systemic; possible skin/eye irritation	Cooling agent; mild irritant
Propylene Glycol	>20000	6 (non-toxic)	Very high	Very high	Inactive for major endpoints; mild irritation possible	Humectant; very safe
Vitamin E	>5000–10000	6	High	High	Inactive; antioxidant benefits	Antioxidant; very safe

The results indicated that most of the compounds fell within moderate to low predicted toxicity classes, although a few ingredients exhibited predicted alerts associated with irritant or sensitization potential. These findings provide a preliminary safety assessment of the evaluated compounds and highlight the importance of computational screening in identifying ingredients that may require further dermatological evaluation for safe cosmetic formulation.

Discussion

The present study applied an integrative bioinformatics approach to evaluate the potential biological interactions of ingredients present in commercial soaps commonly sold in Kaduna markets and their possible implications for melanogenesis regulation and skin health in darker skin populations. The *in-silico* analysis of 43 unique bioactive compounds from 15 commercial soaps prevalent in Nigerian markets revealed a diverse chemical profile, including

surfactants (e.g., Sodium Laureth Sulfate, Sodium Lauryl Sulphate), preservatives (e.g., EDTA variants), fragrances (e.g., Coumarin, Hexyl Cinnamal), and potential modulators such as Hydroquinone, Lauric Acid, Allantoin, and Butylated Hydroxytoluene (BHT) (Table 1). SwissTargetPrediction identified 375 protein targets (probability ≥0.1) for 16 compounds, with enrichment in melanogenesis-related proteins including tyrosinase (TYR), tyrosinase-related protein 1 (TYRP1), and dopachrome tautomerase (DCT), as well as upstream regulators like MITF and associated signaling pathways (e.g., MC1R/cAMP, MAPK, PI3K-Akt, Wnt, Notch) (Figure 2-9, Table 3) (D'Mello et al., 2016; Pillaiyar et al., 2017). KEGG pathway enrichment confirmed significant associations with melanogenesis, tyrosine metabolism, MAPK signaling, and melanoma-related networks (Figure 4–10), suggesting that certain soap ingredients may hypothetically perturb melanin biosynthesis and pigmentation homeostasis.

These predictive findings are particularly relevant for individuals with darker skin phenotypes (Fitzpatrick types V–VI), prevalent in African populations, where higher constitutive eumelanin levels, larger melanosomes, and enhanced tyrosinase activity provide superior photoprotection against UV-induced DNA damage, reactive oxygen species, photoaging, and skin cancer (Solano, 2020; Zamudio Díaz et al., 2024). Potential disruption of these pathways through the inhibition of TYR family enzymes or downstream signaling could theoretically compromise this balance, increasing risks of hypo- or hyperpigmentation disorders with psychosocial significance in black communities (Benn et al., 2016). Notably, Hydroquinone (detected in one product) was flagged as a predicted interactor with tyrosinase-related targets, consistent with its well-established role as a classic tyrosinase inhibitor that suppresses melanogenesis but carries risks of exogenous ochronosis, irritant dermatitis, and heightened UV vulnerability with prolonged use in darker skin (Pillaiyar et al., 2017; Zolghadri et al., 2023). Coumarin and related fragrances showed predicted interactions with pigmentation-linked targets, aligning with some evidence that coumarin derivatives modulate melanogenesis via pathways like PKA/CREB or GSK3β/β-catenin (Kim et al., 2023). Lauric Acid and Allantoin also emerged as recurrent hits for melanin/inflammation-related proteins, consistent with reports that fatty acids influence tyrosinase stability or degradation (Ando et al., 2004).

ProTox-3.0 predictions indicated that most compounds fall within Classes IV–VI (harmful to non-toxic), though alerts for skin irritation/sensitization in fragrances (e.g., Coumarin, Hexyl Cinnamal) and Hydroquinone underscore caution for daily topical exposure (Table 4) (Banerjee et al., 2024). These results highlight how everyday cosmetic ingredients in African-market soaps may hypothetically influence melanogenesis, particularly in contexts where photoprotection is critical.

This study is purely computational and hypothesis-generating, with no molecular docking, molecular dynamics simulations, or experimental validation (e.g., tyrosinase inhibition assays in melanocytes or skin models) to confirm predicted interactions or functional effects. Only 16 of 43 compounds yielded predictions in SwissTargetPrediction, a common limitation for non-drug-like molecules (e.g., simple surfactants, inorganic salts, or fatty acids) that often lack structural similarity to known ligands in curated databases or possess minimal bioactivity data, resulting in no or low-confidence outputs. The lenient probability threshold (≥0.1) was chosen to support exploratory identification of potential therapeutic targets, with noise mitigated by pathway enrichment and biological filtering; stricter cutoffs (e.g., ≥0.5) might have reduced false positives but risked excluding moderate-confidence hits relevant to cosmetic compounds. The sample was market-specific (Kaduna, Nigeria), limiting generalizability to other regions. Few prior studies have applied SwissTargetPrediction or similar tools specifically to commercial soap ingredients, though emerging network pharmacology approaches have predicted tyrosinase inhibitors from natural/cosmetic sources (Jeon et al., 2024; Liang et al., 2025). These predictions therefore require wet-lab validation (e.g., tyrosinase assays in melanocytes, melanin quantification in 3D skin models) to establish causality and practical implications for pigmentation safety.

Overall, this first integrative in silico analysis of African-market soaps underscores the potential of bioinformatics for preliminary cosmetic safety screening and advocates for regulatory attention to high-risk agents like Hydroquinone, while emphasizing the need for experimental follow-up to protect natural photoprotective mechanisms in darker skin populations.

CONCLUSION

This integrative *in silico* analysis reveals that bioactive compounds in commercial soaps widely used in Nigerian markets may hypothetically interact with key melanogenesis proteins (e.g., TYR, TYRP1, DCT) and signaling pathways (e.g., MAPK, PI3K-Akt, Wnt, Notch), potentially affecting melanin biosynthesis. These predictive findings are particularly relevant for darker skin phenotypes prevalent in African populations, where eumelanin provides critical photoprotection against UV damage and skin cancer. The detection of hydroquinone in some products is especially of concern due to its established risks of exogenous ochronosis and increased UV vulnerability in darker skin types. ProTox-3.0 toxicity predictions highlight moderate irritation/sensitization risks for certain fragrances and preservatives. Overall, these results underscore the need for experimental validation and emphasize public health implications for African markets, where inconsistent enforcement of regulations on hydroquinone and similar agents in cosmetics persists despite national bans (e.g., NAFDAC guidelines in Nigeria). Strengthening regulatory surveillance, reformulation of high-risk products, and public awareness could help safeguard pigmentation homeostasis and photoprotection in vulnerable populations.

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