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In Silico Screening of Different Natural Dyeing agent on the Basis of their Efficiency to Stain and Sensitivity to Human Skin

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Abstract

Staining agents or dyes have been widely used in the cosmetic products, and since many years natural dyeing agents has been majorly used in the cosmetic industry. They have been in major use due to their compatibility with the skin and safety profile. In some study it has been observed that even if the product is of natural origin they do have different undesirable effect or side effect. In this research work skin sensitivity of natural dyeing agent was analyzed, Adsorption, distribution, metabolism, excretion and toxicity properties were also analyzed and skin permeability properties were analyzed. All these analysis were done of natural dyeing agents were also studied For this study five natural dyeing agents were chosen Curcumine, Lawsone, Betanin, Juglone and Indigo. An attempt was also made to perform ADME toxicity, skin se so that the gastrointestinal system based compatibility of these agents can be checked and analyzed. The result of these studies exhibited that Betanin and Curcumine are the best and safe coloring agents that can be used in cosmetic industry as per in-silico potential determining study of this research work.

Keywords: In-silico, Toxicity, Betanin, Coloring Agent, Curcumine.

Introduction

Dyeing and colors have been widely used in the cosmetic industry to enhance asthetic appearance. Natural dyes have been used for its safety and benefit of their natural origin. though, the use of synthetic dyes in the nineteenth century has been taken a rrmakabley big market of the existence of these dyes[1].

Betanin is also used as a colorant in cosmetics and pharmaceutical industries .It has been reported to possess benefits of betalains and betalain-rich foods[2]. They are water-soluble containing nitrogen pigments and are subdivided in to red-violet betacyanins and yellow-orange betaxanthins. It is the main red pigment of Beeroot and only approved for use in food and pharmaceutical products as a natural red colorants[3].

The other agent which is majorly used in dyeing industry is Indigo. It has also been used as a dye in Dyeing Industries .It has good color fastness in dyeing [4].

The other natural dyeing agent is Indigo which is a dark blue color dye. It is one of the oldest dye of India from Indigofera family. This plant is well-known for the purpose of dyeing in the textile and printing industry. Indigo powder also acts as a natural hair dye. As synthetic hair dye cannot be a healthier alternative when compared to natural indigo hair dye due to the health of the scalp and hair [5].

Another dye obtained from walnut Juglone showed antimicrobial activity also. It is a naphthoquinone-type dye known as a C.I Natural Brown 7 dye and is also used to dye natural and synthetic fibers[6].

Henna has been used since antiquity to dye skin, hair and fingernails, as well as fabrics including silk, wool and leather. Henna contains a compound called Lawsone. Lawsone (2-hydroxy-1,4-naphthoquinone), also known as hennotannic acid, is a red-orange dye present in the leaves of the henna plant (*Lawsonia inermis*) as well as in the flower of water hyacinth (*Eichhornia crassipes*).

Henna works leaves paste is applied on the hair, Lawsone, gradually migrates into the outer layer of the hair and binding to hair protein creating a fast stain. It does not open the hair cuticle and not cause hair damage, apart from it its skin friendly[7].

The other natural dyeing agent is curcumine obtained from turmeric .It produces yellow color. Curcumin is a dye that can produce high color strength and fastness. It is the best known natural yellow color producer. It produced from the extraction of the Curcuma longa L root and bulb. It was also known as Natural Yellow[8,9]. In research great advances have been made using the QSAR/quantitative structure–toxicity relationship (QSTR) model to predict the acute toxicity of chemicals[10,11]. This good target property of molecules can also confirmed by ADME properties estimation which exhibits probability values of Human Intestinal Absorption, Blood Brain Barrier crossing , Carcinogenic probablity, and HLB value which predict and screen the molecules[13].

All these types properties of natural dies and huge application of Natural dyes was the reason to analyze the staining and dyeing potential of These natural dyes using in-silo screening techniques.

Material and Methods

Following studies were conducted using online open accessible software The software used for the in-silico study was mainly coded in Python 2.7 The process of screening of Natural dyeing agents Curcumine, Lawsone, Betanin, Juglone and Indigo on the basis of Favorable properties like In silico permeability, Insilico Toxicological properties and in silico sensitivity and compatibility of the molecules on the basis of *in-silico* studies.

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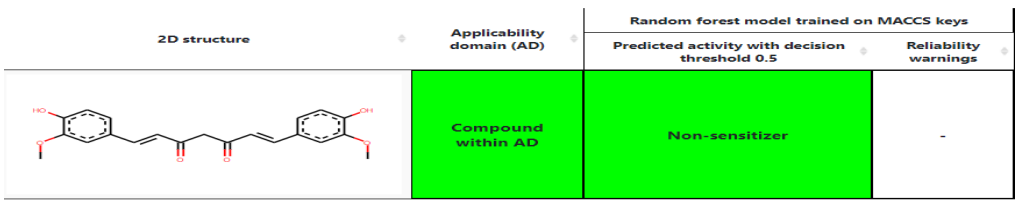
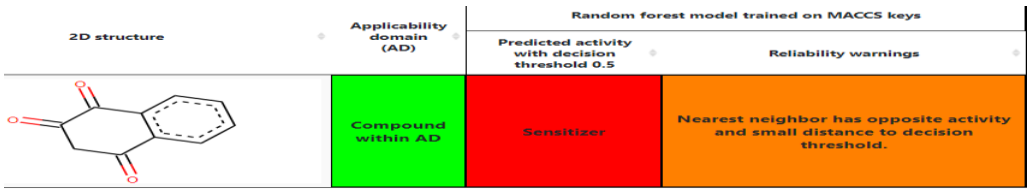
Result and Discussion

Curcumine was analyzed under Applicability domain AD and it was observed None sensitive at threshold of 0.5. Lawsone an staining agent of henna as also observed under Applicability domain and it was observed that it has bit sensitizing agent at decision threshold of 0.5. Betanin obtained from Beet root analyzed under applicability domain AD and it was observed None sensitive at threshold of 0.5. Juglone obtained from Walnut analyzed under applicability domain AD and it was observed sensitive at threshold of 0.5 though Indigo obtained from indigofera tictoria also analyzed under applicability domain AD and it was observed non sensitive at threshold of 0.5.

Betanin showed highest molecular weight 550g/mol as compared to Indigo, Juglone, Curcumine and lawsone .It is also soluble in water .It has low absorption from GI track and no permeability from Blood brain barrier. TPSA Topological polar surface is 249.38 Å^2 and that is why its is soluble in water. Indigo has molecular weight 262.26 g/mol though its topological polar surface area is 65.45 Å^2 and due to which its solubility is less than Betanin. As it says that on increasing hydrophobicity up to some extent also increase drug likeliness property and this is the reason why Indigo has got best skin permeation as compared to other four molecules 5.

ADME toxicity study revealed that Curcumine did not show any sign of Liver toxicity, membrane transporter inhibitor and Inhibition of Metabolism by it .Similarly Indigo has also not shown any sort of Liver toxicity, membrane transporter inhibitor and Inhibition of Metabolism. Juglone obtained from walnut did not show any sign of Liver toxicity .It also did not show any sign of membrane transport based inhibition though metabolism based cytochrome inhibitor for 2c9 transport. Betanin exhibited Liver toxicity and cytochrome inhibition for 2C9 and 2C and 2C19 receptor. Lawsone inhibited 1A2 Cytochrome inhibitor.

Curcumine	
Lawsone	

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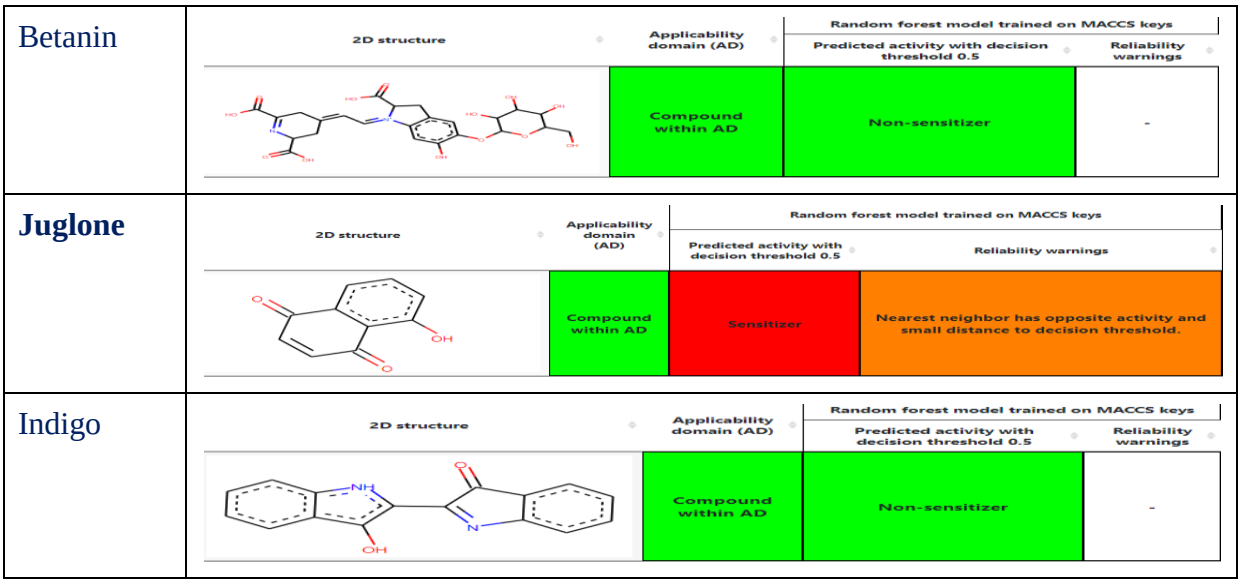

Figure 1.Skin Sensitivity of all the natural dyeing agents used in this study

Table 1.Natural Dyeing Agents and their sources

Indigofera tinctoria containing dye Indigo	
Walnut contain dyeing agent Juglone	
Beetroot contain dyeing agent Betanin	
Henna contain dyeing agent Lawsone	
Termeric contain dye Curcumine	

Table 2.Different properties of natural dyeing agents

Properties	Betanin	Indigo	Juglone	Curcumine	Lawsone
Molecular weight	550.47 g/mol	262.26 g/mol	174.15 g/mol	368.38 g/mol	174.15 g/mol
TPSA	249.38 Å²	65.45 Å²	54.37 Å²	93.06 Å²	54.37 Å²
Log $P_{o/w}$	-3.14	2.63	1.36	3.03	0.96

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Class	Soluble	Moderately soluble	Soluble	Moderately soluble	Soluble
GI absorption	Low	High	High	High	High
BBB permeant	NO	yes	no	no	yes
P-gp substrate	NO	No	no	no	no
CYP1A2 inhibitor	No	Yes	no	no	no
Log K_p (skin permeation)	-10.73 cm/s	-5.96 cm/s	-6.00 cm/s	-6.28 cm/s	-6.76 cm/s

Table 3.Adme Toxicity study of Natural Dyeing Agents

Betanin 1

Query	Liver Toxicity		Metabolism						Membrane Transporters			Others			
				Cyp Inhibitors for											
	DILI	Cyto-toxicity	HLM	1A2	3A4	2D6	2C9	2C19	BBB	P-gp Inhibitor	P-gp Substrate	hERG Blocker	MMP	AMES	MRTD (mg/day)
	Yes	No	⊘	No	No	No	Yes	Yes	⊘	No	No	No	Yes	No	704

Juglone 1

Query	Liver Toxicity		Metabolism						Membrane Transporters			Others			
				Cyp Inhibitors for											
	DILI	Cyto-toxicity	HLM	1A2	3A4	2D6	2C9	2C19	BBB	P-gp Inhibitor	P-gp Substrate	hERG Blocker	MMP	AMES	MRTD (mg/day)
	⊘	⊘	⊘	⊘	⊘	⊘	⊘	⊘	⊘	⊘	⊘	⊘	⊘	⊘	⊘

Lawsone 1

Query	Liver Toxicity		Metabolism						Membrane Transporters			Others			
				Cyp Inhibitors for											
	DILI	Cyto-toxicity	HLM	1A2	3A4	2D6	2C9	2C19	BBB	P-gp Inhibitor	P-gp Substrate	hERG Blocker	MMP	AMES	MRTD (mg/day)
	⊘	⊘	⊘	⊘	⊘	⊘	⊘	⊘	⊘	⊘	⊘	⊘	⊘	⊘	⊘

Conclusion

Betanin and Lawsone exhibited better solubility as compared to Curcumine, Indigo and juglone. The result of the skin sensitivity study revealed that Betanin, Curcumine and Indigo

exhibited no sensitivity to the skin as compared to Juglone and lawsone. If we compare Adsorption, Distribution, Metabolism and Excretion based in-silico study which is as such not a part of dyeing properties on skin but some of these dyeing agents are used in food Industries also excluding betanin all other dyeing agents have shown high absorption. Lawsone and Indigo have shown high Blood brain permeability .Even Indigo exhibited metabolism related inhibition of CYP1A2 along with highest skin permeability. In conclusion It can be concluded that Betanin and Curcumine are the best and safe agents that can be used in cosmetic industry as per insilico potential determining study of this research work.

Conflict of Interest

There is no conflict of interest.

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