ARBUTIN AS A DEPIGMENTING AGENT WITH SKIN LIGHTENING PROPERTIES: A REVIEW

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ABSTRACT

Arbutin is a compound of hydroquinone and D- glucose extracted from bearberry plant, Alpha-arbutin and Beta-arbutin both are the derivative of hydroquinone. Beta-arbutin found in several plant species whereas Alpha-arbutin obtain by biotransformation, there have been serious studies on skin lightening and hyperpigmentation action of this substance. Arbutin and it's derivative have been studied for their melanin synthesis inhibitory action.
The efficacy of arbutin is alone or in combination with other active ingredient, combine therapy of arbutin with laser enhance the depigmentation efficacy. Arbutin rarely cause dermatitis when use in excess.
It hopes that this review will help to understand the advantage and disadvantage of arbutin.

Keyword: - *Alpha-arbutin, Skin lightening agent, Hyperpigmentation, Melanin, Dermatitis.*

1. INTRODUCTION

1.1 Hyperpigmentation

Hyperpigmentation is a condition which is including melasma[1], Post inflammatory hyperpigmentation[2], it also caused by the UV radiation[3], Dyschromatosis is another condition which is hypo or hyperpigmented skin[4].
It occurs due to changes in biochemical cycle which controlling melanogenesis, Melanogenesis is hard and complicated process by which melanocytes produce melanin in melanosomes[5].

Fig -1: Melasma and Hyperpigmentation

1.2 Melanin

Melanin is polymeric coloured pigment distributed in every part of skin, hair, eye and other body tissue, Melanin synthesize in melanosomes, Melanosomes are the unique organelles located in melanocytes [6] [28].

Melanocytes shows different activity in individuals but density of melanocytes is not too much different in individuals [7] [29].

1.3 Regulation of Melanin Synthesis

Melanin synthesis is affected by the various factors like Genetics, Environmental factors, Nutritional factors, Hormonal changes etc[8] [30].
For example propiomelanocortin derived peptide hormone like Alpha-MSH (Melanocytes stimulating hormone) Beta-MSH and adrinocorticotropic hormone, which act as agonist for the melanocortin-I receptor, A GPCR (Gaba-protein-coupled-receptor) and stimulating protein kinase leading the activation of CREB (cAMP response element binding protein)[9] [8].
Active CREB binds to cAMP response element on the promoter of MITF (microphthalamia-associated transcription factor)[10] [31].
MITF plays an important role in the regulation of Melanin synthesis [11] [8] [9].

1.4 Melanin Synthesis Pathway

Melanin synthesis starts with oxidation of L-tyrosine to DOPAquinone by oxidation of L-3,4 dihydroxyphenylalanine (DOPA) to DOPAquinone [12] [32] [33] [34].
DOPAquinone reacts with cysteine and form 5-S-CysteinylDOPA or 2-S-CysteinylDOPA enters in the pheomelanin synthesis pathway, these two compounds oxidised quinone by cyclization and produce benzothiazine and benzothiazole intermediate which used in the synthesis of phenomelanin[13].
Alternatively when DOPAquinone is oxidised to DOPAchrom in lack of cysteine DOPAchrom converted into DHICA in the presence of TYRP-2 (Tyrosinase-Related Protein-2) and further converted into DHICA melanin in the presence of TYRP-1 (Tyrosinase-Related Protein-1),
These are used to synthesis the Brownish- Black polymer Eumelanin[14].

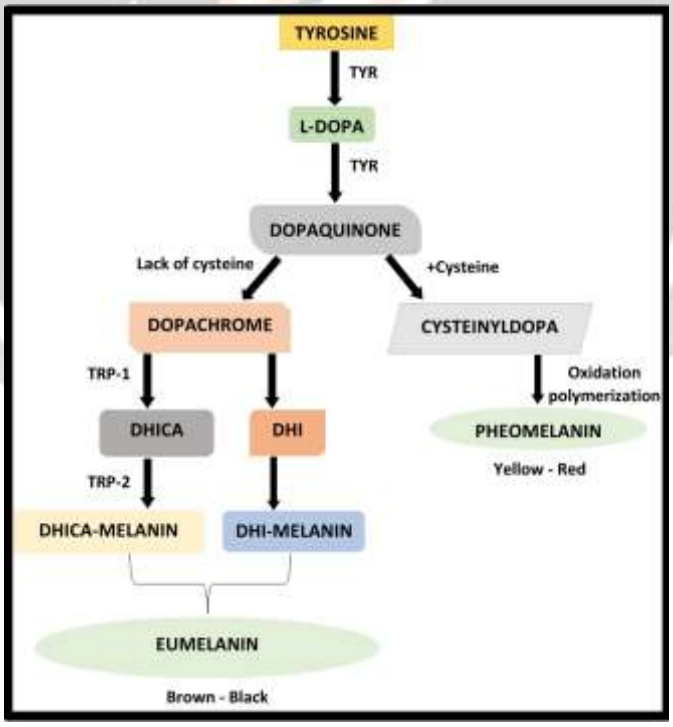

Fig -2: Synthesis of Melanin

2. ARBUTIN

Arbutin is a derivative of hydroquinone (hydroquinone-O-B-D-glycopyranoside) and found in bearberries, cranberries, blueberries, wheat and pears[15] [35] [36].

Arbutin (Alpha-arbutin and Beta-arbutin molecular weight 272.25 Da) and appears as a white to off white powder and has a melting point between 195-197°C and boiling point 561.6°C ± 50°C[16].

The solubility of alpha arbutin in water and dimethylsulfoxide is 151 g/L at 20°C ± 5°C and 54 mg/ml (198.34mM)[17].

Arbutin has highly hydrophilic log p value = -1.49, So it is low to penetrate into the skin[18]. Arbutin is resistant to light and unstable in highly acidic environment (pH=2), Arbutin go under partial hydrolysis in presence of water in hydroquinone which can be oxidised into benzoquinone[19].

Arbutin is an effective treatment of hyperpigmentry disorder and also used as a skin lightening agent, Arbutin shows less melanotoxicity than hydroquinone [20].

The effect of arbutin compared to it's mother compound, hydroquinone could be attributed to the glycosidic bond needs to be cleaved prior affecting tyrosinase[21]. The synthetically produce derivative of arbutin, deoxyarbutin has been shown effective and safe skin lightening agent[22].

Compared the effect of hydroquinone, arbutin and deoxyarbutin and found that all three compound had similar inhibitory effect on tyrosinase activity [23] [35] [23] [37].

Fig -3: Chemical structure of Alpha arbutin & Beta arbutin

2.1 Antimelanogenic Effect of Arbutin

Arbutin has effect of reducing Melanin level at 0.1 and 1.0 mM concentration that has little effect on viability of cultured human melanocytes showed that arbutin dose dependently reduce TYR activity in human melanocytes at concentration 0.1 and 1.0 mM, and it's inhibitory effect against cellular Melanin synthesis is more potent than kojic acid or L- ascorbic acid when compared at fixed concentration (0.5mM)[24].

Arbutin shown to inhibit Melanin production in B16 cells stimulated by Alpha-MSH abolish the hyperpigmentation effect of Alpha-MSH in Human skin[25].

The decrease in TYR activity in human melanocytes by arbutin doses not appear due to decrease in expression level of this enzyme [20]. Arbutin lowered cellular melanin content but did not reduce the protein level of TYRP, TYRP-1 and TYRP-2[27].

It is considered that arbutin as an inactivator of cellular TYR[28]. It has been reported, arbutin can also act as substrate TYR in the presence of catalytic of L-DOPA as a cofactor, arbutin oxidised by mushroom TYR to produce 3,4-dihydroxyphenyl-o-beta-D-glucopyranoside[29].

The results showed that hydroquinone derivative arbutin suppressed melanin production by inhibiting TYRP-1, TYRP-2.

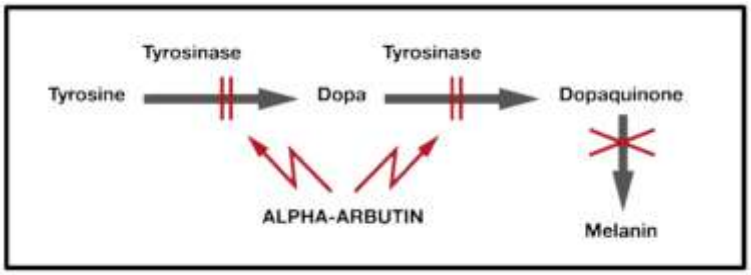

Fig -4: Mechanism of Action of Arbutin

3. RECENT ADVANCEMENT IN ARBUTIN DELIVERY TO SKIN

Alpha-arbutin is one of the best skin lightening agent having less toxicity in comparison to hydroquinone.
It is hydrophilic in nature because it having -1.49 log p value that's why it having poorly permeate into skin.
To enhance the permeation across the skin, there is an urgent demand to improve permeation and penetration in the skin by developing various Novel Drug Delivery System like Microsystem. Lipid system etc.

4. MARKET OVERVIEW OF ALPHA-ARBUTIN

Alpha-arbutin generally use for skin lightening, age spots and hyperpigmentation treatment, Alpha-arbutin seen increase demand in pharmaceutical industry, which makes highly profitable opportunity.

North America has the large number of consumer of Alpha-arbutin.

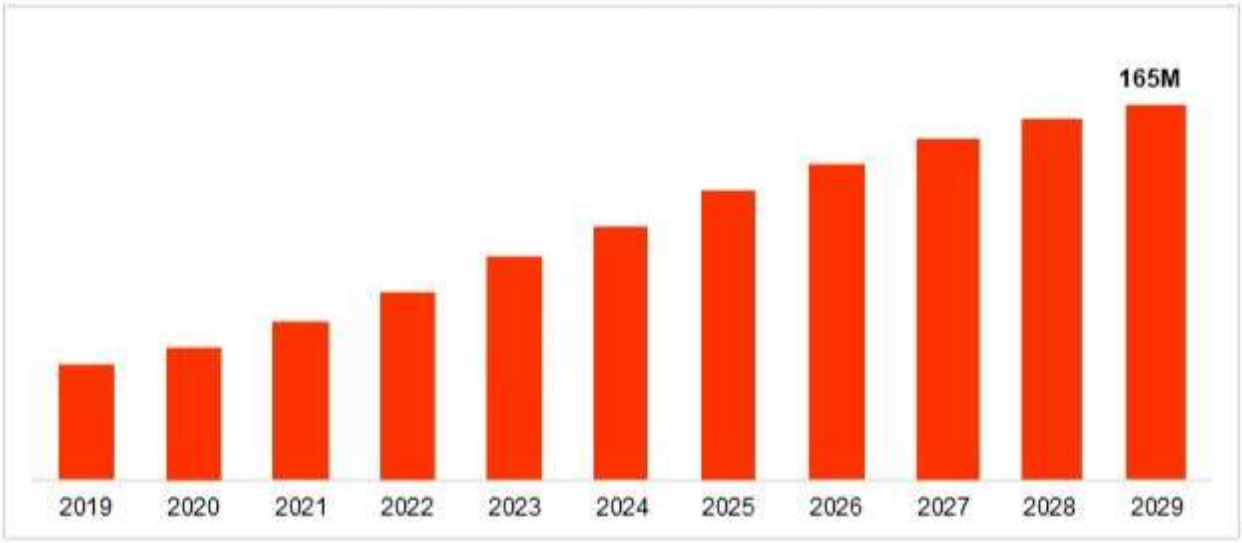

Chart -1: Global arbutin market data 2019-2029

4.1 Arbutin Market Scope

Metrics	Details
Base Year	2020
Historic Data	2018-2019
Forecast Period	2021-2028
Study Period	2018-202/8
Forecast Unit	Value (USD)
Revenue Forecast in 2028	USD 165 Million
Growth Rate	CAGR of 7.2% during 2028
Region Covered	North America, Europe, Africa, South America

Table -1: Arbutin Market prediction

4.2 Key Markets player

- Huaheng Biotech
- Bondong chemical
- Adina cosmetics ingredient

4.3 Highly Consumer Region

- North America
- Europe
- Asia Pacific
- Latin America
- Rest of the word

5. CONCLUSION

In Conclusion, Arbutin found highly effective and less toxic, that's why arbutin emerged as a popular alternative of other harmful skin depigmenting agent because of it's outstanding capability to reduce hyperpigmentation.

Now a days Arbutin leading on top due to massive growth in cosmetic and pharmaceutical industry.

Initially Arbutin have some drawback like poor penetration and permeation but today's scenario scientist developed various types Novel Drug Delivery System such as Microsystem, Lipid System .

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