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Essentials Of Trichophoric Designing

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Abstract:

Psychosocially, hair related pharmaceuticals have become the promising life style drugs. They prevent hair loss and promote dense as well as glowing hair. They improve modern youth's social charm and psychological appeal. Hair cosmetics are the beautifiers of human personality. To achieve this the chemical parameters of hair trichophore should be delineated. A model of androgenic hair trichophore has hypothetically derived. It is made up of heteroatoms (H-bonding), Aryl,heteroaryl, alkyl, alkenyl (Vander wal interaction)Steroidal conjugated >c=o, hydroxyl for hydrophobic and H-bonding and anagen phase stimulators (Naturalproducts e.g Capsicum,Niacin,Ursolic acid and Bio-flavonoids.

1.Introduction

The hair biology revealed that the hair follicle's activity is cyclical for the growth. The migration of stem cells to hair matrix initiates mitosis and differentiation. It is controlled by cytokine produced by cells of dermal papilla. Some follicular and dermal papilla cells have androgen receptors in their cytoplasm and nucleus. Therefore hair growth is hormonal event[1-5] and androgen dependent. Androgens indirectly control hair growth by affecting synthesis and release of cytokine from dermal papilla[6]. The cytokine produced by cells of the dermal papilla is keratinocyte growth factor (KGF) which induces extensive hair growth in murine models of alopecia. Receptor for KGF is found in keratinocytes in basal epidermis. Insulin like growth factor[7].(IGF 1) hastens growth of hair and hair follicles in a concentration dependent manner. IGF-1 binds with the proteins produced in the dermal papilla cells to form IGFBP-3 (insulin like growth factor binding protein complex)[8].It is responsible for hair elongation and maintenance in the anagen phase.Retinoids and glucocorticoids stimulate production of IGFBP-3 in dermal papilla cells[6-7]. Capsaicin (chili pepper)[9-11] releases substance P from nerve endings in skin. It induces transition of hair from telogen to anagen phase. Growth of androgen dependent hair is influenced by :

- Declined androgen biosynthesis.
- Blocking testosterone transformation to 5-alpha-DHT (Dihydrotestosterone).
- Blocking androgen receptor.

2.Theoretical Methodology

Many drugs have profound effects on hair growth in humans. The drugs can effect both androgen dependent and androgen independent hair[1-5]. They either cause hair loss (hypotrichosis)[12-14] or promote hair growth (hypertrichosis)[6,15].The drugs enhancing hair growth of androgen dependent hair drugs are testosterone, anabolic steroids, glucocorticoids, minoxidil diazoxide, phenytoin, carbamazepine and cycloserine. Certain drugs inhibit mitosis in matrix cells (telogen effluvium).They are cytotoxic drugs (alkylating agents and alkaloids)etc vitamin A heparin , interferons, anginotensin converting enzyme blockers, propranolol, metaprolol, trimethadone, levodopa, nicotinic acid, salts of gold, lithium, cimetidine amphetamine, isoniazid, ibuprofen and salicylic acid.

The chemical and biological diversities of hypertrichotic and hypotrichotic structures directed new strategy for designing the hair growth promoter molecules. The concept of

"hair trichophore" analogous to pharmacophore is elaborated. In order to do so, the ideal qualifications of hair growth promoting structures were deliberated on the basis of the reported literature.

- Blood circulation enhancer
- Anti-inflammatory or anti-bacterial
- Enzyme activator
- Proliferation stimulator (mitosis accelerator)
- Rejuvenator(regenerate growth potential)
- Growth factor enhancer or releaser
- Optimal lipophilicity for topical application

The physicochemical and structural entities for hair growth agonism and antagonism should be deduced to design new hair growth promoter type of life style drugs. To achieve this objective the structure of follculoid should be thoroughly known. It has been investigated by co-culture technique using hair follicle cells and dermal papilla cells[17].The result of these cell culture studies gave uncertain information about hair growth stimulation. The specific structural moieties of hair trichophoric character were derived from.

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- Aliphatic planarity
- Conjugated carbonyl
- Hetero atoms especially aza and oxo with lone pair of electrons
- Aryl or hetero-aryl Alkyl groups

The androgen dependent hair growth requires the steroidal agonism,therefore nuclear structure should have receptor complementarity. The hair growth efficacy was introduced by replacement of carbon of rings A and B at 4 or 6 positions by "aza atom"

and imparting enzyme inhibitory action on DHT with elevation in andronergic anabolism. The reported SAR of azasteroids[18] supports the derivation of structural moieties for androgenic hair growth stimulation.

Planarity,lipohilicity ,vasodilatory and growth potentiator factor are basic components for the androgenic hair trichophore design. The quality of possessing color is noticeable in compounds containing certain well defined chemically unsaturated groups called chromophores or color bearers which are not equally effective in producing color.Majority of hair oils have aliphatic chromophoric and aromatic lipophilic structural combination. Their role in hair coloration is not well defined,although they may contribute to lusture and styling of hairs.

The chemical structures of hair and androgen receptor lead to design the androgenic hair trichophoric agonist assigning possible biophoric sites for interaction with hair growth promoter molecules.

The structural features,essential for hair growth agonism are:

- Heteroatoms (O,N) with lone pair of electrons for h-bonding.
- Planar,hydrophobic (sp2 character dominance) aryl,heteroaryl,alkenyl and alkynyl functions which contribute to receptor binding affinity through vander wal interactions.
- Structural features which stimulate release of endogenous hair growth stimulation factors .Many natural products are anagen phase stimulators[9,10,19].

Pottasium channel openers[20,21] also elicit hypertirichosis and share almost the same structural moeites as described before in trichophore design.The experimental data concerning potassium channel openers suggested that they maintain differentiation of hair keratinocytes culture and stimulate proliferation of cells in culture vibrissae and skin keratinocytes. The tests in vitro suggested that P-1075 and cromakalim are more potent than minoxidil,pinacidil and nicorandil. Their trichogenic capacity to regenerate anagen in human follicles is significant for hair growth. The anti hair growth structures cause hair loss or inhibit hair growth. They have hypertrichogenic moieties which are capable of mitosis inhibition in matrix cells (anagen effluvium).

3.Result

The designed trichophore for improving the hair growth products stimulate androgen and K-channel receptors.It can be concluded that molecular association or hybridization of

structural moieties having following bioactions may evolve new strategy for hair growth promoter molecules.

- Produced endogenous nitric oxide
- Enhance mitosis in follicular and dermal papilla cells.
- Promote nutrients supply by enhancing blood circulation.

The proposed trichophoric designing probably be useful in promoting efficacious hair growth structures of therapeutic promise for the life style drugs.

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