Aetiology and treatment of epidermal depigmentory disorder in humans

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The epidermal depigmentary trigger in humans at post-natal level may occur with the toxification of skin organ with the endogenously produced melanocytotoxic hydrogen peroxide and subsequent formation of hydrogen peroxide- melanolipoprotein conjugate involving the hydrogen bonding of complementary hydroxyl and carbonyl molecular surfaces of these biosignitures respectively. The condition is multifactorial but reversible. The structural and functional degeneration of melanocytes under the acquired condition never occur. The molecular conjugation theory on the aetiology and line of treatment of the epidermal depigmentary disorder (recoined as hepato-epidermal syndrome HES) has been proposed. The inherent sulfoxides of *Allium cepa* have been found as the renaturant of HES condition with the capacity to dislodge the denaturant hydrogen peroxide forming stronger hydrogen bonding with hydrogen peroxide than that of carbonyl molecular surface of melanolipoprotein, the epidermal colour determinant. The orally and topically defined plant based combined therapy advances the recovery time of HES condition.

Keywords: Hydrogen peroxide- melanolipoprotein conjugate, Hepato-epidermal syndrome, Sulfoxides loaded antioxidants Human skin coat repigmentation.

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INTRODUCTION

The UVB directing skin faculative colour biodispensed photobiologically at peri-natal level over and above the integumentally defined constitutive colour determined at pre-natal level, in line with the timeline strategy of evolution and natural selection is a key to the survival of human life upon earth at post-natal level. This biodispensation prevents the visit of the UVA and UVC directing skin cancer. In 1994 Sawhney[1] defined the skin faculative colour as melanolipoprotein -a heteropolymer of melanin (a homopolymer of 5, 6-indolequinone) and lipoprotein in preference to melanin alone due to its thermal instability at about 31^0C. The human skin colour has been defined and determined in the timeline of evolution and natural selection in line with the regionally defined UV index[2,3] (0-10) as the ultraviolet radiation impacting epidermally determines the skin coat tone at peri-natal and post-natal level over and above the integumentally defined light skin wrap at peri-natal level. The asymmetric nature of human skin coat tone of human population worldover appears to be proportionate to the quality, quantity and intensity of UVB impacting upon population in line with the regionally defined UV index.

The African incubatory had been the natural selection for the evolution of human life upon earth. The human life emerged upon earth initially assumed dark skin coat. First, the human life has been blessed with the gene directing light skin integumental wrap at pre-natal level which is further layered epidermally at peri-natal level with the faculative colour triggered biosynthetically in the melanocytes activated photobiologically with the interface of UVB under the impacts of ultraviolet radiation at the tropical lines (UV Index □6-10) subsequent to the clinically defined blood level of 30+ng/ml of vitamin D_3 biosynthesised in stratum spinosum and stratum basale on the absorption of UVB by the inherent deposits of 7,

de-hydrocholestrol in these layers. The functional trigger to melanocytes occurs with the interface of radiation with the cells bioplaced and biospaced beyond stratum basale. The UV radiation travel beyond stratum basale is conditional upon the rise of the clinically defined blood level of vitamin D_3 as 30ng/ml. Unlike human life, the animal skin coat colour and pattern is gene directing and biodispensed once at pre-natal level. The European races were once dark skinned, but with their settlement in the habitates with the regionally defined UV index (0-5) they assumed fair complexion as compared to the races along or on the tropical lines. The pre-natal skin coat status of European races shows no signs of change at peri and post-natal level unlike the neonatal born on or near the tropical lines as the regionally defined conditions (UV index 0-5) fail the sun directing bioprocesses to occur in the skin organ.

The experience points to the lasting character of the skin colour aging with the age of human life upon earth. The recent incidents of epidermal depigmentary disorder (called EDD, henceforth) in humans over the last 50-60 years down the lane have failed the strategies of the timeline of evolution and natural selection. The trigger on the onset of epidermal depigmentation in humans with progression to generalised depigmentary condition has been found as refractory. Instead of the proposed autoimmune mechanisms[4], cytotoxic mechanisms[5], theory of intrinsic defect of melanocytes[6], oxidant-antioxidant mechanisms[7], and neural mechanism[8] on the aetiology of epidermal depigmentary disorder in humans, the precise cause remains unknown. The attempts have been made to understand the factors responsible for the epidermal depigmentary disorder, and the line of treatment basing upon the sulfoxides loaded biosignitures of *Allium cepa*.

MATERIAL AND METHODS

The blood samples of 11 adults (7 females and 4 males) aged 24-30 years were involved in this study. Two single blind experiments involving one normal healthy adult (age 25) and a EDD patient (age 30) with the topical application of 1% ethanolic solution of hydroquinone upon the

pigmented parts (1″x1″) of their bodies, and a female adult with moderate complexion (age 30) with the oral administration of a Nutrizex capsule sourced from Hilife Nutrients New Delhi India per day (composition lutein, lycopene, calcium pantothenate, vitamin B_6, copper sulphate, folic acid, chromium chloride, vitamin B_{12}, vitamin D_3, sodium selenate, biotin) were conducted .

The 70% ethanolic extract of the powder of shade- dried leaves of *Lawsonia inermis Linn* was prepared in line with the procedure adopted by Chaudhary[9]. The filtrate was evaporated to dryness under reduced pressure by rotory evaporation. The 10µg of the solid powder was administrated orally per day to two EDD patients.

The aqueous extract of *Allium cepa* was obtained by refluxing the contents for 24 hours. The decanted aqueous solution was reduced to ¼ of its original volume to obtain the aqueous concentrate. The aqueous concentrate of *Allium cepa* was daily applied topically at night upon the depigmented part of the EDD patient.

RESULTS

The topical application of 1% ethanolic solution of hydroquinone for 40 days on the pigmented parts of the normal healthy subject and EDD patient depigmented the skin coat area involved. The hydroquinone directing depigmentations of the parts involved were kept under observation for next 60 days. The depigmented part on the skin coat of the normal healthy subject assumed renaturing, renormalisation and rehabilitation with restoration to the original skin coat colour after 20 days, but the depigmentation on the part of the skin coat of EDD patient persisted and showed no sign of repigmentation like that of healthy normal subject, even after 60 days.

The female of age 30 with moderate complexion (Fig1a) fed on a Nutrizex capsule per day for 60 days assumed dark complexion (Fig1b). In another single blind experiment, the oral administration of 10µg of the powder of *Lawsonia inermis Linn* leaves used in Ayurvedic system as an alternative medicine for curing different diseases, to EDD patient aged 35 years

resulted in the trigger of repigmentation which showed the signs of relapse on withdrawing the dose.

The blood levels of vitamin D_3 and folic acid of 11 volunteers having asymmetric skin complexions (fair to black) ranged between 4-12ng/ml (normal range; 20-31ng/ml) except one (a non-vegetarian) who showed marginally true value of vitamin D_3 (□20ng/ml) whereas the blood level of folic acid of all was registered within the normal range of the vitamin (3-17ng/ml) except one, the dark skin female of 28 years (shown in Fig 2b) who had the highest blood level of folic acid as 32ng/ml. In Fig 2a and 2b are shown the representative data on two females with fair and dark complexion respectively. The topical application of the *Allium cepa* on the white patches on the human body of the patient (age 42) daily at night for 12 hours for 40 days helped trigger the repigmentation with progression to the normal skin coat colour (melanolipoprotein). In Fig 3a and 3b are exhibited the skin coat status before and after the application of aqueous concentrate of *Allium cepa.*

Before intake of Nutrizex After intake of Nutrizex

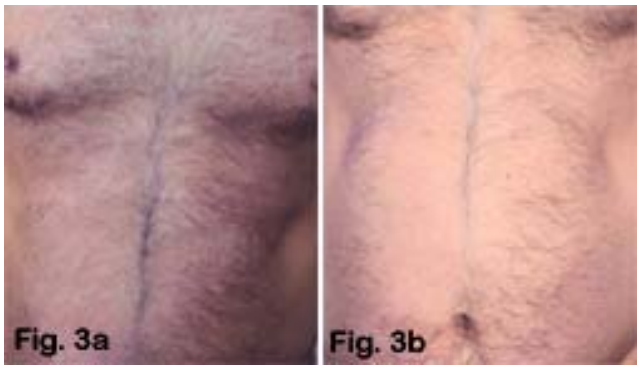
Age 24 Age 28

Follic acid = 11ng/ml Folic acid = 32 ng/ml

(Normal = 3-17ng/ml)

Vitamin D_3= 12ng/ml Vitamin D_3= 7.2 ng/ml

(Normal = 20-31ng/ml)



Before topical application of aqueous concentrate of *Allium cepa*

After topical application of aqueous concentrate of *Allium cepa*

DISCUSSION

Melanolipoprotein- a heteropolymer of melanin (homopolymer of 5, 6-indolequinone) and lipoprotein, determines the human skin coat colour at post-natal level. Its lasting character at post-natal level is conditional upon the continuous detoxification of the human system hepatically, renally, intestinally and epidermally and the perfect synergy among the bioplaced and biospaced body organs in biobartering the required organics biostrategised in the timeline

of evolution and natural selection in order to arrest the toxin(s) including free radical level(s) going beyond the carrying capacity of the body system. The toxification of the body system may invite the occurrence of the signs of body degeneration with culmination to unnatural happings in the body. The hydroquinone directing depigmentation of skin coat faculative colour (melanolipoprotein) of the selective parts of the normal healthy subject and EDD patient may result in with the formation of hydroquinone-melanolipoprotein conjugate involving intermolecular hydrogen bondings at the complementary molecular surfaces of hydroquinone (-OH) and melanolipoprotein (□C=O) as shown in Fig 4. The renaturing, renormalisation and rehabilitation of the selective skin coat white patch of the healthy normal subject within 20 days on discontinuation of the topical application of hydroquinone solution was a pointer to the perfection in the hepatically defined biosynthesis of purging protein and its exchange to skin organ enabling it to hydrogen bond hydroxyl groups of the exogenously introduced hydroquinone toxin in the skin matrix more strongly than that of carbonyl groups of the melanolipoprotein, and to sweat off ultimately the hydroquinone-purging protein conjugate. The depigmentation caused by hydroquinone on the selective parts involved on the body of EDD patient failed to respond to time like that of normal healthy subject suggesting the depression and suppression in the inherent detoxification mechanism of skin organ, conditional upon the hepatically defined exchange of purging protein to skin organ. The epidermal depigmentary disorder may be recoined as hepato-epidermal syndrome (HES) in the light of the organs involved in preference to the earlier misnomers used thereon.

The recent reports by Karin U[10-11] et al., on the overproduction and accumulation of melanocytotoxic hydrogen peroxide endogenously beyond the carrying capacity of the melanocytes or the body extend the support to the concept of body toxification as the root cause of HES condition. The hydrogen peroxide like hydroquinone may conjugate the melanolipoprotein in melanocytes, stripping it of its natural normal character, and triggering the

onset of the epidermal depigmentary disorder with the progression to generalised HES condition. The H_2O_2- melanolipoprotein conjugate is shown in Fig 5.

The empirical treatment basing upon plant-based psoralene- UVB therapy has shown the encouraging repigmentation responses in the HES condition as registered by different researchers[12-22] The author also observed repigmentation response with the oral therapy using 10µg solid powder of *Lawsonia inermis Linn* leaves containing 2-hydroxy 1, 4-naphthaquinone as the principal ingredient, a relative of menadione[23] (2-methyl- 1, 4-naphthaquinone) which has been found to mimic the vitamin K activity in the body, suggesting the vitamin K role in the biosynthesis of melanolipoprotein in melanocytes. These responses put to rest the earlier claims on the death, functional and structural degeneration of melanocytes under HES condition. The darkening of the skin coat of the female of moderate complexion with the oral intake of a Nutrizex capsule for 60 days replete with antioxidants and vitamins, and the higher blood level of folic acid of dark skinned female aged 30. (Fig 1b) suggested on the relevance of antioxidants and folic acid in defining skin coat faculative colour, its epidermal biostabilisation, and the line of treatment of HES condition.

The *Allium cepa* directing renaturing, renormalisation and rehabilitation of HES condition may be assigned to the capacity of sulfoxides loaded inherent biosignitures known as antioxidants like allicin (2-propene-1-sulfinothioic acid S-2-propenyl ester), alliin (2R)-2-amino-[(S)-prop-2-enylsulfinyl] propanoic acid), S-alkenyl-L-cystein sulfoxide, n-butyl-tri-fluoroacetyl-S-1-propyl-L-cystein sulfoxide, S-1-methyl-L-cytein sulfoxide, trans- S-1-propenyl-L-cystein sulphoxide and other as reported by David J. Thomas [24]. The negatively charged oxygen covalently bonded to the positively charged sulphur on the molecular surfaces of cystein sulfoxide derivatives, and oxygen double bonded to sulphur on the molecular surfaces of Allicin, Alliin exhibit more electronegativity than that of oxygen covalently double bonded to carbon on the molecular surfaces of 5,6 indole-quinine (the part of melanolipoprotein), forms stronger hydrogen bonding as described by Bruce[25] with the

complementary hydroxyl group of H_2O_2 dislodging the conjugated H_2O_2 from the H_2O_2-melanolipoprotein conjugate under the body condition on the topical application of the aqueous concentrate of the white onion bulbs, and subsequently freeing the colour determinant (melanolipoprotein) epidermally. The representative conjugate structures of H_2O_2 and the principal predominant ingredient of *Allium cepa* (alkenyl-L- cystein sulfoxide and Allicin) are shown in (Fig. 6, 7). The other antioxidants like allanine, alpha-tocopherol, B-carotene, cholesterol, cystein, diallyl-disulphide, diallyle-trisulphide, histidine, kaempferol, catechol, oleonolic acid, p-coumeric acid, palmitic acid, protocatechuic acid, quercetin, rutin, sinapic acid inherent in *Allium cepa* may act as adjunct to the activity of sulfoxides. The oral intake of aqueous extract of onions (*Allium cepa*) together with the topical application of aqueous concentrate of A*llium cepa* on the white patches may help advance the recovery time of renormalisation of HES condition, as the antioxidants of A*llium cepa* may help improve upon the bodily enzymic activities mimicing inherent SODs and catalase, and to eliminate and neutralise the overproduction of free radicals including H_2O_2 which have been held responsible for the precipitation of HES condition. The other phytochemicals of *Allium cepa* as reported by different workers [26-39] like vitamins A, K, B_9 (folic acid) etc may biostabilise the renatured melanolipoprotein epidermally.

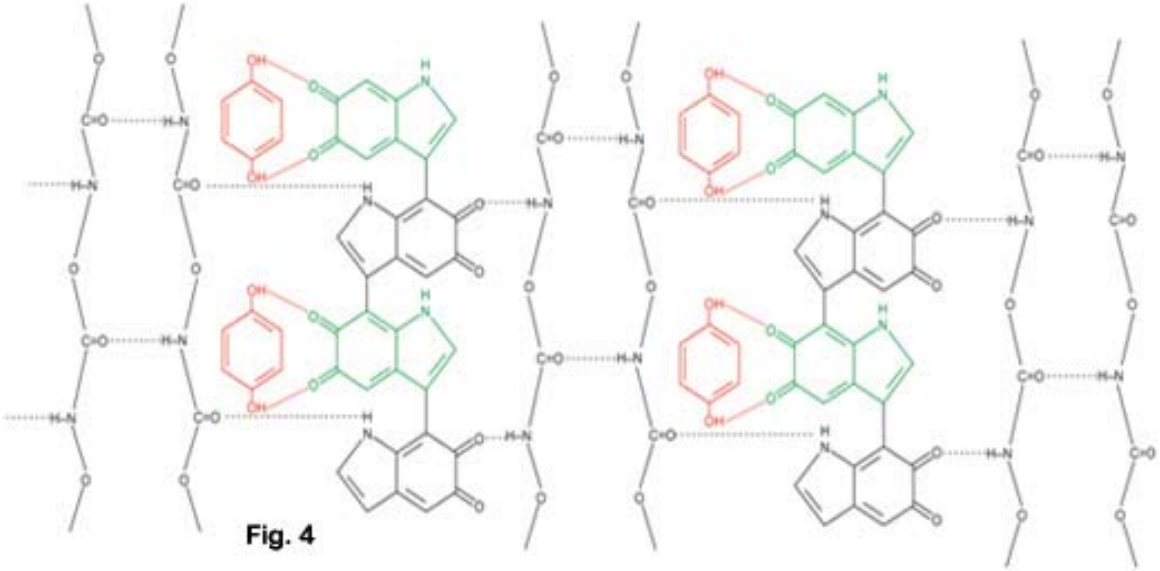


Fig. 4

Hydroquinone melanolipoprotein conjugate-The triggering molecule of HES condition

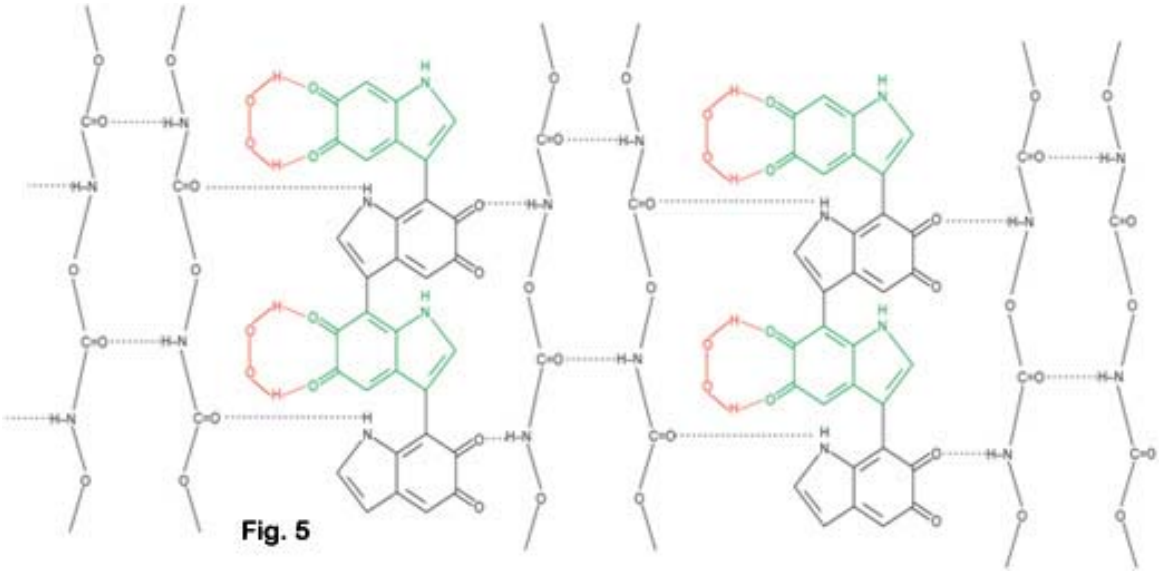


Fig. 5

H_2O_2-melanolipoprotein conjugate-The triggering molecule of HES condition

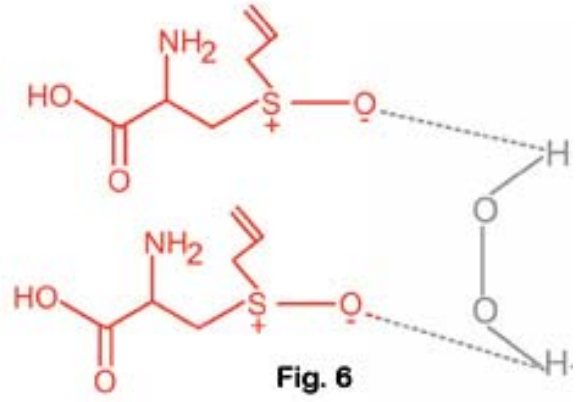


Fig. 6

H_2O_2- Alliin conjugate

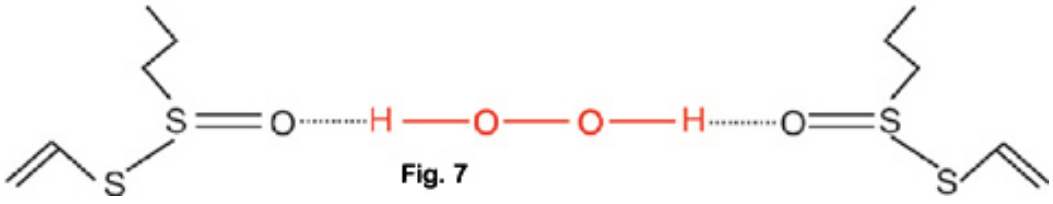


Fig. 7

H_2O_2- Allicin conjugate

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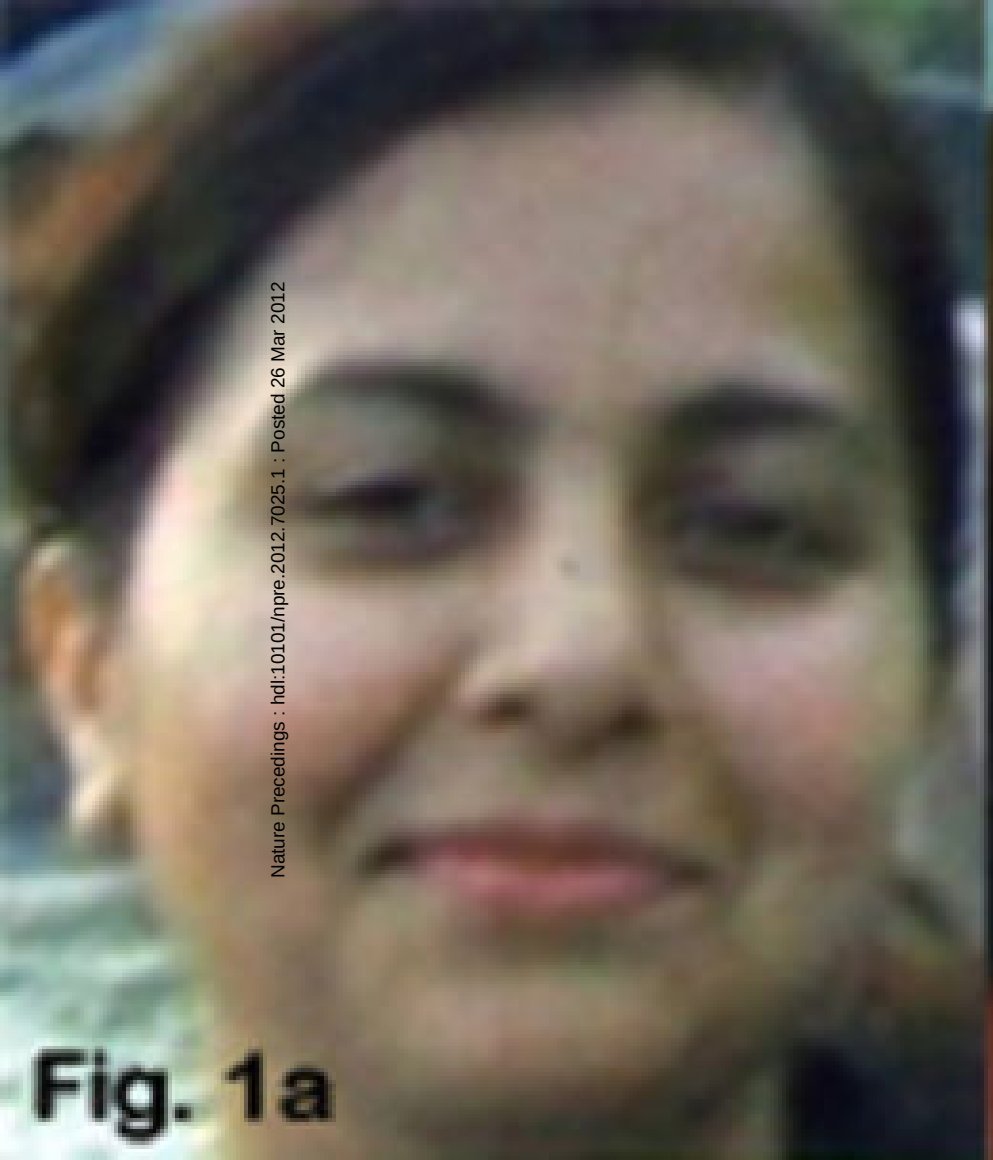

Fig. 1a

Fig. 1b

Fig. 2a

Fig. 2b

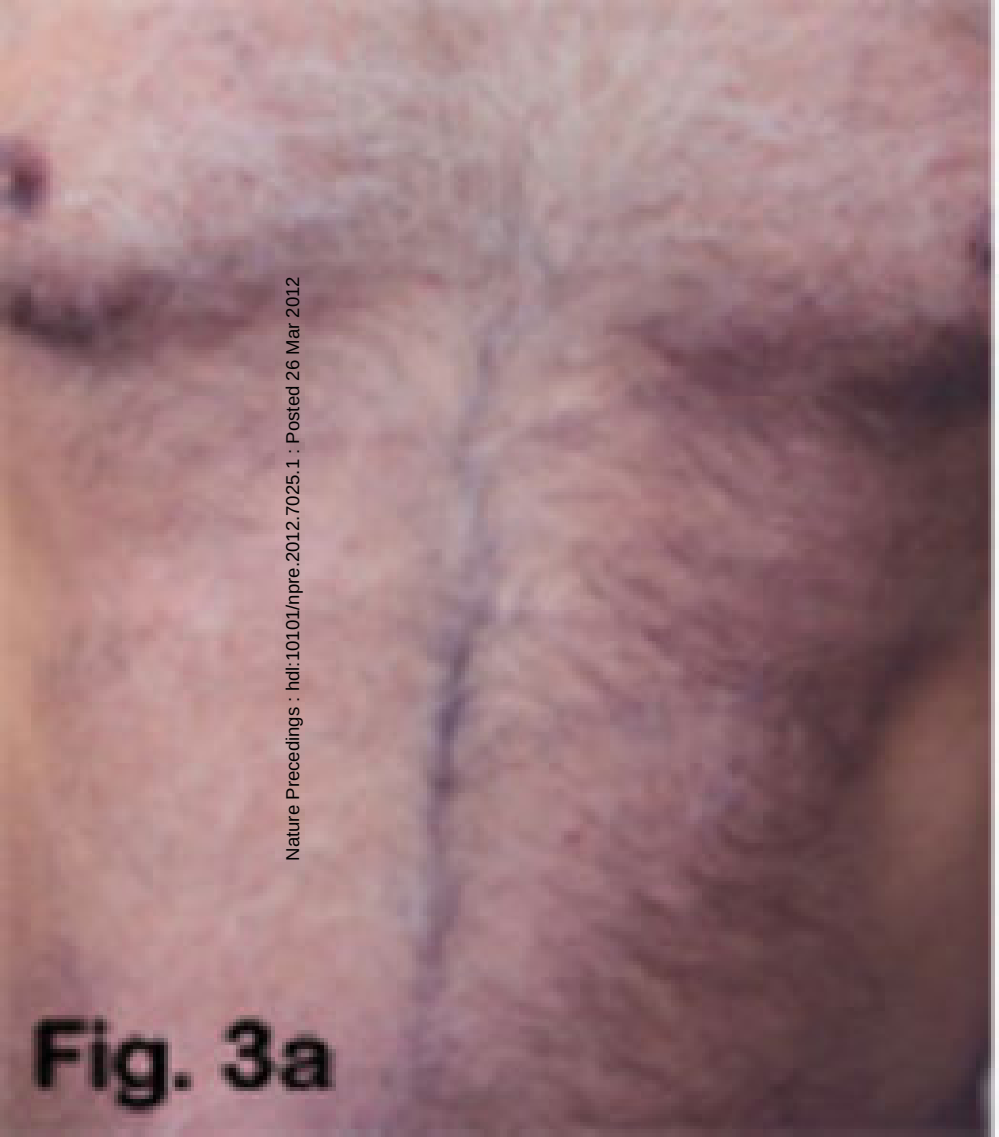

Fig. 3a

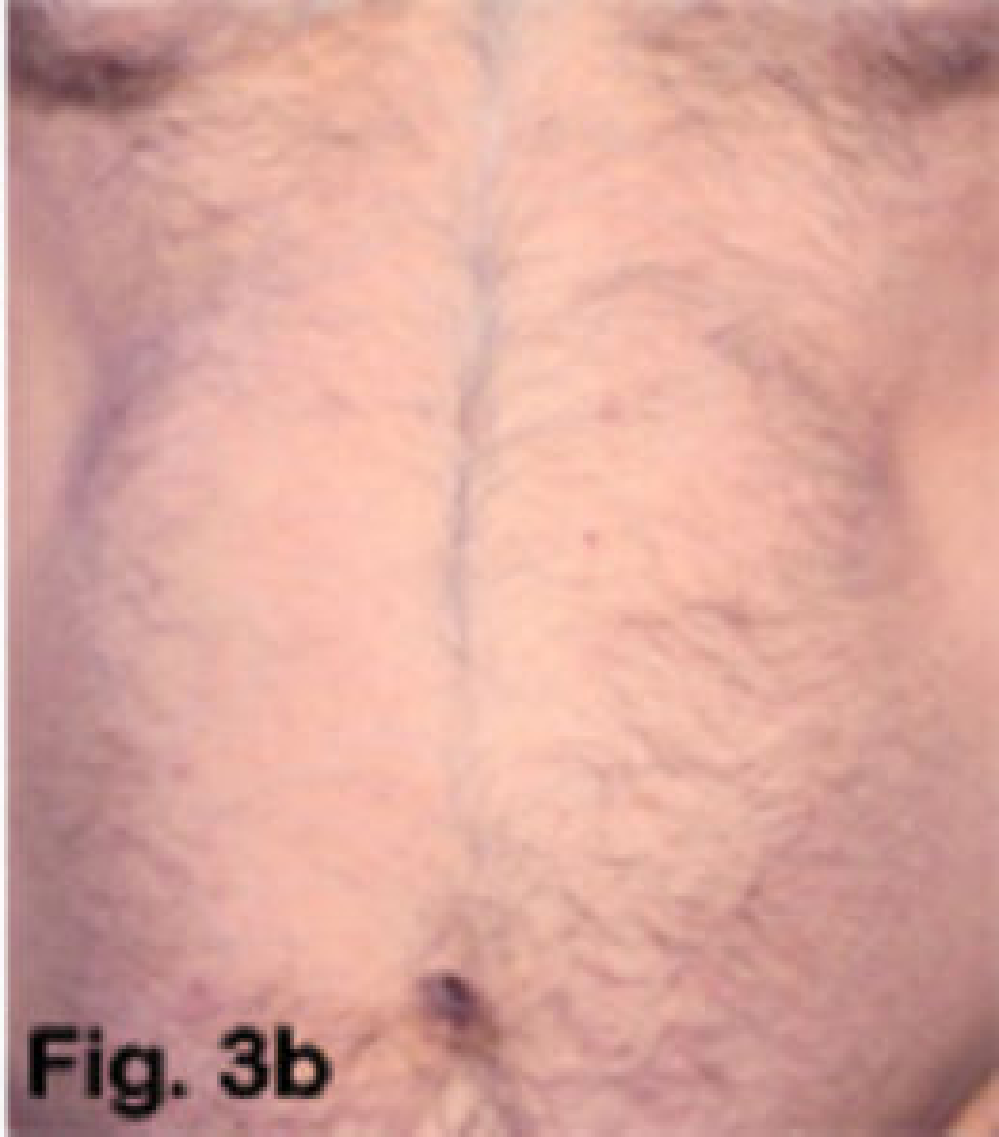

Fig. 3b

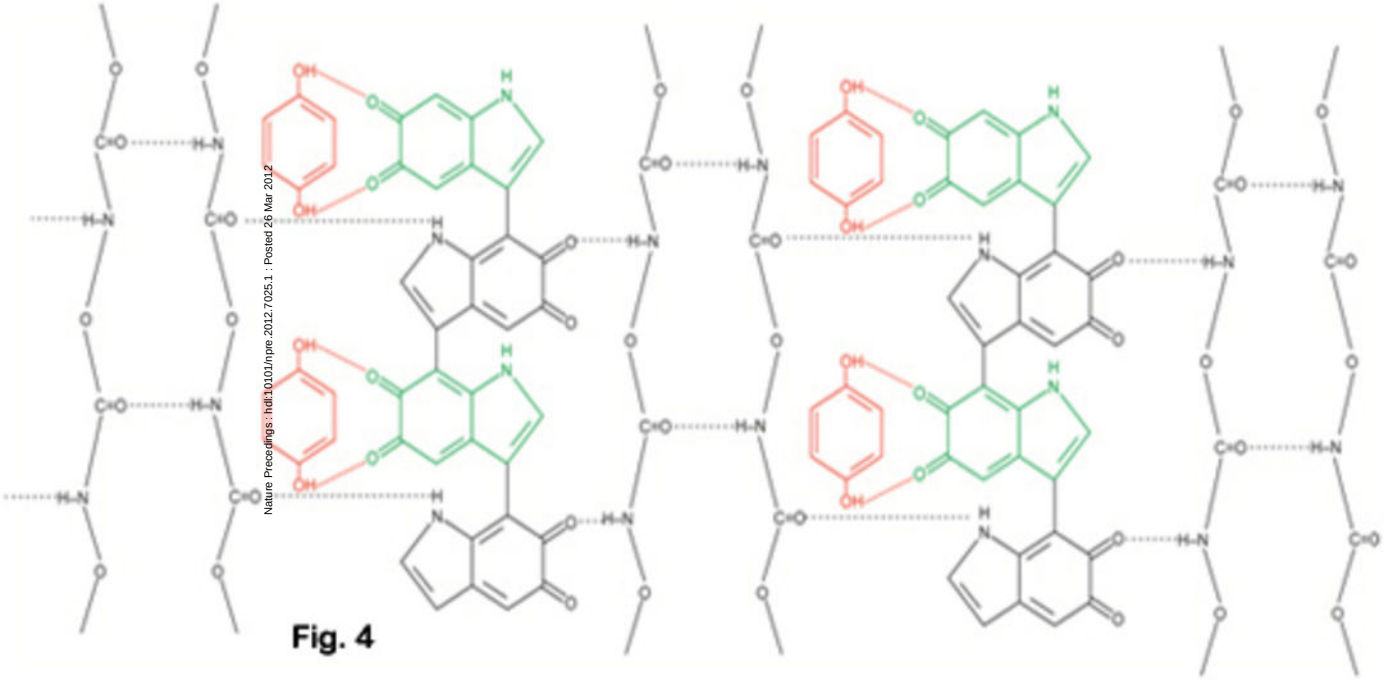

Fig. 4

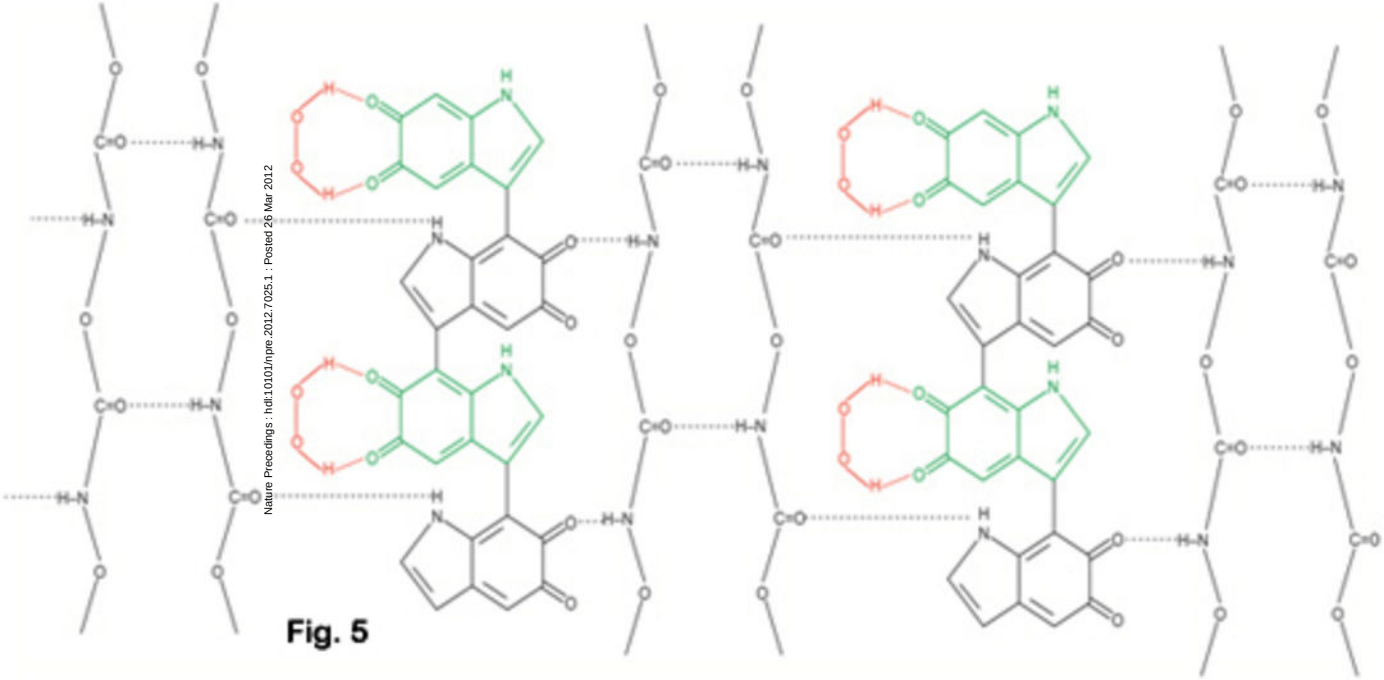

Fig. 5

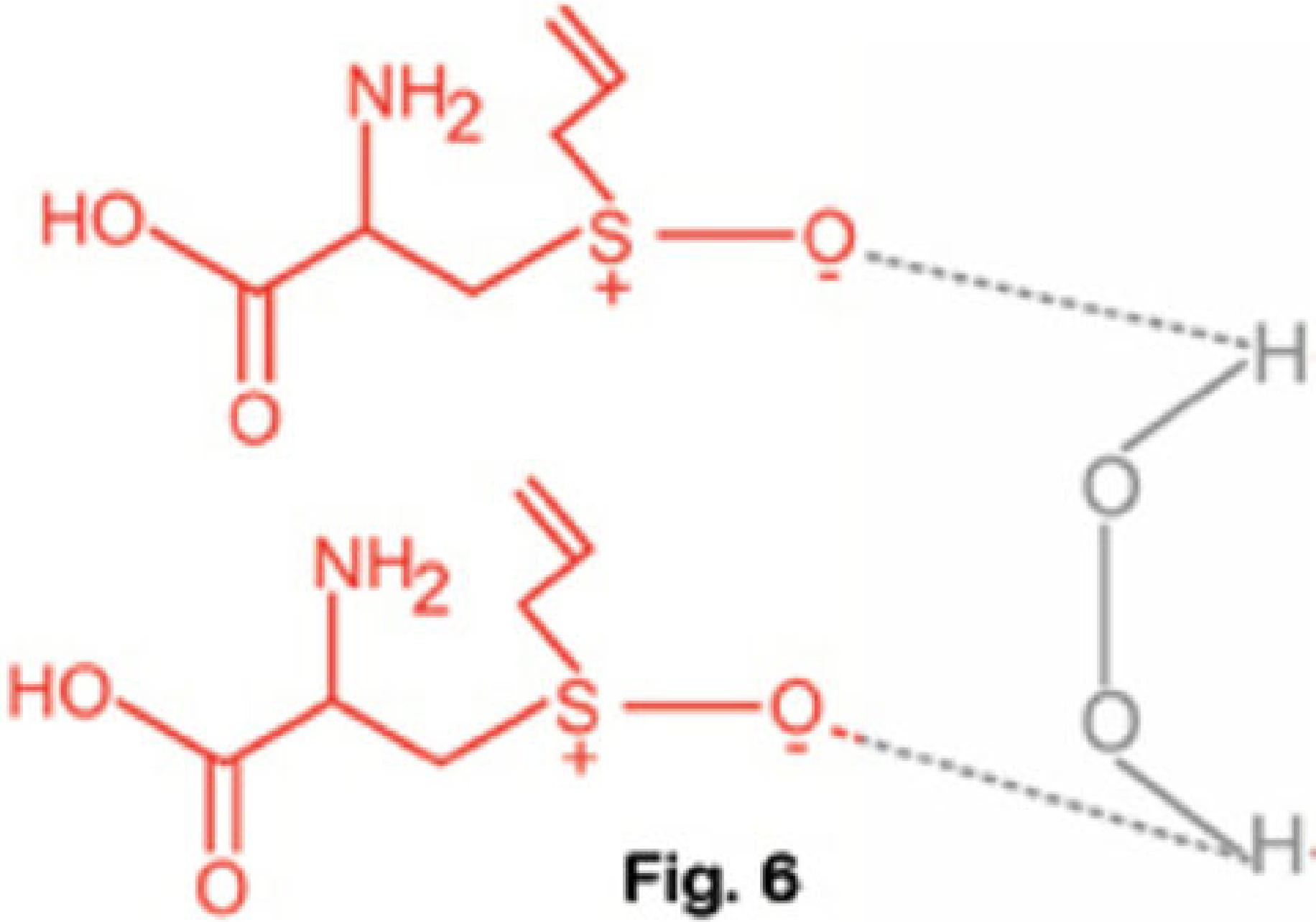

Fig. 6

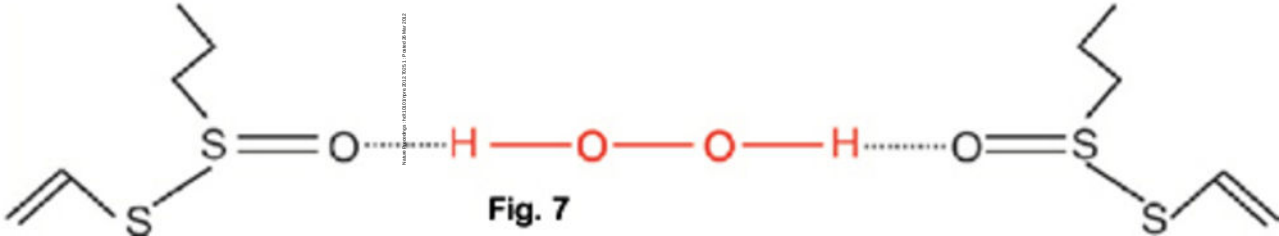

Fig. 7