World Journal of Pharmaceutical and Life Sciences
WJPLS
www.wjpls.org
SJIF Impact Factor: 6.129

CRACKING *HOMO SAPIEN* SKIN PIGMENTARY ORDER, AETIOLOGY OF SKIN DEPIGMENTARY DISORDER AND ITS ATTENDANT SKIN CANCER OR CANCER AND THEIR REHABILITATION WITH NAPHTHOQUINONE THERAPY

Dr. S. S. Sawhney*

Research and Development (R& D) Division, Department of Chemistry, Uttaranchal College of Science and Technology, Dehradun – 248001 (Uttarakhand) India.

***Corresponding Author: Dr. S. S. Sawhney**
Research and Development (R& D) Division, Department of Chemistry, Uttaranchal College of Science and Technology, Dehradun – 248001 (Uttarakhand) India.

Article Received on 02/12/2019 **Article Revised on 23/12/2019** **Article Accepted on 13/01/2020**

ABSTRACT

Introduction: The black *Homo sapien* prototype at tropics, relevant to earthly conditions, had been evolved under the sapient biostrategy of natural selection, but with a code. The skin depigmentary disorder among non- European black Asian, African and Australian at tropics, and the assumption of light- toned integumental coat by white European at beyond tropics are the evolutionary defiances. The aim of this study is to unravel and crack the mechanisms thereof, and rehabilitate the skin depigmentary disorder among the *Homo sapiens*. **Methods and material:** Fourteen Asian Indian consented and volunteered for this study. Complete Body Scan Analysis was conducted on nine volunteers. Four HES patients were treated topically or orally or both with vitamin K_1 or naphthoquinone precursors to vitamin K_2 *(Plumbago Zeylanica L.*), followed by exposure of relentless sun high intensity UVB. A normal female volunteer was put on the dose of 10g of Walnut Karnels of *Juglons regia* L. for a year in addition to her staple diet, followed by exposure of relentless sun high intensity UVB. **Results:** The interplay of the epidermal vitamin K threshold and the relentless sun high intensity UVB has been identified as the mainstay of the skin pigmentary order as defined in black *Homo sapien* prototype at tropics. The vitamin K deficiency in *Homo sapiens* has been identified as the skin depigmentary disorder precipitant, whereas the relenting sun low intensity UVB precipitates light – toned integumental coat among the *Homo sapiens* at beyond tropics. These evolutionary defiances among *Homo sapiens* result in the maximization of their vulnerability to skin cancer or cancer. The vitamin K based Naphthoquinone Therapy offers new options for the treatment, prevention and pre-emption of skin depigmentray disorder or cancer. **Conclusion:** The vitamin K has been identified as the pro skin pigmentary order, anti-skin depigmentary disorder and anti-cancer vitamer. The supplementation of staple diet with plant -based highly photosensitive and UVB- harvesting 1, 4-naphthoquinone derivatives: root powder of *Plumbago zeylanica* L and fruits of *Juglona regia* L, is strongly recommended to keep skin depigmentary disorder and cancer at bay.

KEYWORDS: *Homo sapien*, vitamin K, melanolipoprotein, skin pigmentary order, skin depigmentary disorder, skin cancer.

INTRODUCTION

All the ecosystems upon earth had been gene - directing with the defined skin - tones with inherent characteristics to resist UVR whereas *Homo sapiens* had been conceptualized, evolved and developed in two phases: Gene - directing pre - natal phase where the gene - directing architectural biodesign of organal ecosystem and networks with light- toned integumental coat as a wrap, defined with the missing inherent potential to resist UVR, and relentless sun high intensity UVB - directing evolution of epidermal facultative pigmentation, which biolayers the pre-natal light-toned integumental coat as a continuum at post - natal level as a protective shield against UVR. The two steps bio - strategy thereon *Homo sapien* evolution under the laws of evolution, unlike other ecosystems upon earth, had been a mystery to humanity and scientists worldover. Had *Homo sapeins* been evolved like other ecosystems upon earth under genetic mode, there would have been far less health – related problems than what is being encountered today by *Homo sapiens* (aka modern humans). Inspite of defined endowment under evolutionary laws, there is no escape but to accept the challenges of *Homo sapien* life upon earth.

The naturally defined *Homo sapien*, fully characterised and equipped with its adaptability, survivability and sustainability to last its bioage upon earth, is an

unparalleled ecosystem upon earth. The *Homo sapien* skin pigmentary order, and depigmentary disorder are the grey areas and esoteric in nature beyond the understanding of humanity till date. The global statistics based upon DNA Kit available at various sites such as *Mapmygenome or 23andMe,* conclusively reveal that the modern humans spread over the whole earth, are all mixed and are descended from a single woman in Africa, having left behind ancestors in Ethiopia, Middle East and Central Asia. Genealogy more than history reminds us that the modern humans came from the same place (Africa) and were once black .A recently analysed DNA sample from a 10,000- year-old skeleton discovered in Gough's Cave near Cheddar Gorge, England, offers a remarkable possibility: the first modern but white British people had once dark brown to black skin. This is no surprise to the scientists as the research presented at the American Association of Physical Anthropologists showed that the whiteness or paleness of light-toned Europeans is only about 10,000 year old. The world's greatest anthropologists, palaeontologists, genealogists, archaeologists and others involved in the science, skipping over the holes in the expansive and inexact Theory of Migration of *Homo sapiens,* connected the dots, navigated the routes tentatively and strung together evidence, speculation to arrive at conclusions-out of which some stood the test of time, agreed that *Homo sapiens* took their outbound steps from Africa- the natural choice part of earth under laws of nature for the conceptualisation, evolution and development of *Homo sapiens* under the defined protocol, including the relentless sun- driven high intensity UVB and temperature 43^0- 46^0C etc. Life on earth has been evolving for 3.8 billion years and our planet has yet to produce a perfect species. This would not stop people from trying.

The *Homo sapiens* schlepped across the whole earth beyond tropics, populating it over the time since their introduction upon earth 2 lac years ago under laws of nature at tropics and the environmental conditions: relenting sun - driven low intensity UVB and lower temperature: < 43^0-46^0C etc, defying the naturally defined protocol for the *Homo sapien* bioconstruct at tropics. The *Homo sapien* multiplication upon earth had been slow initially. The first 1,00,000 years saw the *Homo sapien* population as about 10,000 only since its introduction at tropics which multiplied incrementally in the next 50,000 years, and has grown to 7.6 billion in recent years with their global spread (tropics and beyond), beyond the carrying capacity of earth. The human history tells us that the whole human race (*Homo sapien* at tropics and beyond) continued living under natural conditions with no degenerative signs with black skin - tone as defined under the laws of nature till about 7^{th} century . Over the 10,000 – 15,000 years down the lane since 2019, the signs of black skin - tone degeneration among *Homo sapiens* at tropics have been noticed to the surprise of the scientists. The European races with black skin - tone earlier, had assumed the signs of degeneration to the point of pre- natal light-toned integumental coat (white skin - tone) sans epidermal pigmentation, defined under laws of nature. Surprisingly the tropically defined Asian, African and Australian races have also shown the signs of the trigger of skin depigmentation with progression to generalisation. The incidences of human skin depigmentation is on increase at tropics alarmingly. In India about 10% Indian suffer from the skin depigmentary disorder in stark contrast of other tropically defined races where the signs of this disorder stands at 1-2%. The continuation of this trend among black Asians and African races may engulf them over the period of about 50 years up the lane, like the tropically defined Australians. The so called modernity has been found as the key contributing factor to the uncalled and untold miseries to *Homo sapiens*. The statistics on *Homo sapien* pointed out that over about 1,90,000years up the lane since their conceptualisation under laws of nature, they had been closer to nature without any sign of body abnormalities whatsoever. The modern humans encountered, over about 10,000 years down the lane, the microbially, bacterially, virally and environmentally defined diseases in stark contrast to the Neolithic tribes- the recent find: *Sentinelese* in North Island, a part of 29 Andaman and Nicobar Islands (descendants of black *Homo sapien* prototype, unaffected by modernity) with resistance to modern day diseases and pathogens, and continue to live disease-free life under natural conditions in these islands.

The *Homo sapien* over the last 200 years down the lane with inherent intelligence and enquiring qualities as defined under laws of nature, could advance innovatively and technologically in biosciences and sciences with insights into the coded mechanisms of *Homo sapien* system, slipping into the age of so called modernity. The unveiling of the hidden truths on *Homo sapien* system is welcome and acceptable but the injudicious applications against the naturally defined causes of humanity upon earth: CRISPER - based gene editing – an challenge to evolution, and radioactivity – driven nuclear weapons – an early call to doomsday of humanity upon earth etc, would impact humanity adversely beyond description with the astronomical rise of incurable health- related problems of unknown origins. Time has come to rethink on, and revise the roadmap on closing into the natural conditions drawn under laws of nature earlier. The *Homo sapien* skin depigmentary disorder among black non - European Asian and African races has been found as a recent attribute of modernity which has raised more health - related questions that it has answered. The humanity has to race back to nature if it has a desire to live disease - free longer life upon earth. The skin depigmentary disorder- a global problem now- is no disease per se, but a scientific issue and a defiance of laws of nature at tropics, which has also been encountered in white European who has migrated and settled at out of tropics with relenting sun- driven low intensity UVB in stark contrast to the naturally defined

protocol for the conceptualisation of *Homo sapien* at tropics with relentless sun- driven high intensity UVB.

The light - toned integument coat, as seen in the patients of skin depigmentary disorder, and white European offers free access to UVR to penetrate the skin matrices beyond the epidermal and dermal limits, damaging and denaturating the DNAbases - driven proteins - the building materials for the biodesign of organs: liver, brain, heart, kidney, spleen, pancreas and skin etc - the key to the *Homo sapien* functionality. The direct connection of *Homo sapien* skin depigmentary disorder and skin cancer, consequent to denaturation of the proteins - basic to *Homo sapien* system under laws of nature, is an obvious deduction. The zero – vulnerability of *Homo sapiens* appears to be conditional on the rehabilitation of skin depigmentary disorder among the humanity. *Homo sapien* system had been defined at tropics genetically and earthly to the point of perfection to survive its biotime, as defined under laws of nature, of 100 years upon earth. The filtered scientific experiences pointed to that this system functionality rested upon tripod of gene- directing biosynthesis of proteins, plant - based and chlorophyll loaded biosignatures or precursors to the non - essential biomolecules, and relentless sun - driven high intensity UVB at tropics. The recent advances in sciences and technology helped decode some of mechanisms and the hidden truths thereon, but *Homo sapien* skin pigmentary order among the black Asian and African races at tropics-a relentless sun directing natural feat, and its defiance among *Homo sapien* has not been decrypted so far. The veiled facts thereon the skin related issues including skin depigmentary disorder need to be unveiled to meet out the challenges of natural defiances among humans at tropics and beyond.

A great amount of research has been done on the subject to prevent the defiance of evolutionary laws among humans at tropics. The skin depigmentary disorder is refractory and not gene- driven. The protocol(s) tried so far on the treatments of conditions in reference, have responded poorly with no promising responses. The wild hypotheses[1-4] have been proposed on the aetiology of the skin depigmentary disorder, but no leads on the skin conditions which predispose this unnatural conditions, have been registered so far. Sawhney,[5-7] in 1994 showed structural instability of early held skin colour determinant: melanin- a homopolymer of indole-5,6-quinone at blood heat, and revised it as a conjugate of melanin and lipoprotien : melanolipoprotein- a naturally defined skin colour determinant, and reported in 1996 on the genesis of cutaneous depigmentation induced by chemicals like hydroquinone, p-benzyloxyphenol, p-hydroxypropiophenone and amylphenol with a common hydrogen donor group, and working expansively on the subject reported in 2012 in *Nature Proceedings* on a new term: Hepto- Epidermal Sundrome (HES) – a reflection of hepatic aberration on skin as signs of depigmentation- in preference to early defined misnomers thereon as leucoderma and vitiligo. El Mofty.[8] in 1968, described the therapeutic values of photosensitive psoralens: Ammoidin (8- methoxypsorolen), Ammidin (8-isoamylinoxypsoralen) and Majudin (5-methoxypsorolen) in the treatment of depigmentary disorder (HES) enriched the field of therapeutic and investigative dermatology. Taketsugu.[9] et al. in 2005 reported on the mechanism of skin tanning in different racial or ethnic group in response to ultraviolet radiation. Preston and Stern,[10] in 1992, Kricker[11] in 1994 and Halder[12] in 1995 considered the epidermal facultative pigmentation over and above the pre - natal constitutive light - toned integumental coat, as the protective factor against skin cancer development, following UVR, stating that the constitutive skin – toned coat dramatically affects the incidences of different types of skin cancers. Xiao,[13] et al. Medison,[14] Rees,[15] Kallais,[16] and Meridithet[17] et al. studied human skin determinant and its related factors, highlighting its relevance in *Homo sapien* system.

In 2003 Alison,[18] *et al*. reported on the elucidation of the mechanisms by which vitamin K elicit their activity, and a number of vitamin K – dependent proteins which have been identified in a variety of human tissues including liver, brain, kidneys, heart, spleen, lungs, uterus, placenta, thyroid, thymus, testes and bones, establishing vitamin K universality in *Homo sapien* system. The medical science missed out on the vitamin K role in skin organ. The guesstimate suggested that the nature could have also defined vitamin K role in the skin organ in defining *Homo sapien* skin pigmentary order (HsSPO). Preliminary studies done on the repigmentation of pigmentless skin patches under this study with vitamin K_1 confirmed the guesstimate thereon, resulting in the development of Naphthoquinone Therapy to contain *Homo sapien* skin depigmentary disorder (HsSDD) and *Homo sapien* skin cancer (HsSC) or cancer (HsC) with the use of vitamin K, the derivatives of 2-methyl-1,4-naphthoquinone, and plumbagin (5- hydroxy-2- methyl-1,4-naphthoaquinone), the major ingredient of root powder of *Plumbago zeylanica* L. In 2012, Datta and Mishra[19] reviewed the curing of aging and ill – effect by the use of rejuvenating and anti- aging *Plumbago zeylanica* L as a drug. The shade dried root of this plant bestows strength, intelligence and longevity. The standard dose recommended as per The Ayurvedic Pharmacopoeia of India, the Controller of Publications Delhi, India, 1990, is 1 – 2 g twice a day. Among all its chemical constituents, plumbagin, also known as 2- methyl juglone or plumbagone as the major ingredient with more than 1% in the root, having the characteristic high photosensitivity and UVB – harvestibility (280- 320 nm). The root powder has the wide application in the treatment of lifestyle diseases and disorders. The plumbagin is also a forerunner to vitamin K_2 in vivo in the intestinal track of *Homo sapien* system. The literature survey has shown that the naphthoquinones including vitamin K have not been used as anti HsSDD and HsSC and HsC. The naphthoquinones have been exploited,

highlighting HsSPO with leads on the aetiology of HsSDD, HsSC and HsC and their treatment. Sawhney.[20,32] et al. have studied extensively the hydroxylnaphthoquinones, widely spread in nature: plumbagin,5- hydroxy-2-methyl-1,4-naphthoquinone (*Plumago zeylanica L.*), lawsone, 2-hydroxy -1,4, naphthoquinone (*Lawsonia enermis*), juglone, 5-hydroxy -1,4- naphthoquinones (*Juglans regia* L) and lapachol, 2-hydroxy-3-(3-methyl-2-butenyl)-1,4- naphthoquinone (*Hondroanthus inpetigenosu)*, which act as forerunners to vitamin K_2 in-vivo and behave like vitamin K characteristically, having inherent characteristics of high photosensitivity and UVB - harvestability.

Inspite of the best efforts invested into, the factors and the mechanisms involved in the determination of *Homo sapien* skin pigmentary order remains coded, calling more studies to addess the issue, the resolution of which shall role out definitely the aetiology of *Homo sapien* skin depigmentary disorder (HES condition) prevailing among black non - European Asian, African and Australian, who have become more vulnerable to skin cancer or cancer under the acquired skin conditions. The white Europeans, with the light - toned integumental coat showed parallel skin characteristics to that of HES patients. The scientists are still long way of finding treatment for skin depigmentary disorder and its attendant skin cancer or cancer. Under this study the naturally defined mechanism on the *Homo sapien* skin pigmentary order defined with a code under the evolutionary laws, with leads on the aetiology of skin de-pigmentary disorder and its attendant skin cancer or cancer, and the effective protocols to contain them, have been effectively attended to and addressed. The whole study has been carried out humanely and ethically.

MATERIALS AND METHODS

For cracking the bioscheme defined under natural selection on black *Homo sapien* prototype and the leads thereon the aetiology of skin depigmentary disorder or HES and its attendant skin cancer or cancer, the nine healthy Asian Indian (Fig 7: H8 – H16) and a generalised Asian Indian HES patient (Fig 7: H6) were subjected to the Complete Body Scan Analysis with reference to phenylalanine (Phe), intestinal bacteria index, vitamin K and skin melanin index (= skin melanolipoprotein index) with the non - invasive Japanese Quantum Resonance Magnetic Health (JQRMH) Analyzer. For topical application the vitamin K viscous liquid was used without further purification. The ethanolic extract of root powder of *Plumbago zeylanica* L. was obtained applying usual simple procedure. The 5g of extract was mixed with 95g of moisturizing cream and the contents homogenised to obtain 5% w/w topical formulation. Standard dose of 2g of root powder of *Plumbago zeylanica* L to HES patients was recommended in line with the established Indian Ayurvedic System and Indian Pharmacopoeia of India, the Controller of Publication Delhi, India.

Fifteen volunteer participants were enrolled into the study at the campus of Uttaranchal College of Science and Technology, Dehradun (Uttarakhand) India. All participants provided written consent to take part in the study. The whole study has been done humanely and ethically.

An Asian Indian healthy normal female of 33 years of age was recommended a dose of 10g of Walnut Kernels (*Juglans regia* L.) twice a day in addition to her staple diet for 12 months (Fig 1:H1), followed by exposure of relentless sun high intensity UVB for 07 minutes daily between 10am – 11 am. The skin pigmentless patches of the Asian Indian male of 16 years of age (Fig 2:H2) was daily massaged into with vitamin K_1 viscous liquid repeatedly, followed by exposure of relentless sun high intensity UVB for 07 minutes between 10am – 11 am for 06 months whereas the white patches of 25 years old female Asian Indian HES patient(Fig 5: H5) was massaged into daily repeatedly with 5% w/w ethanolic extract of root powder of *Plumbago zeylanica* L. in moisturizing cream, followed by daily exposure of relentless sun high intensity UVB for 07 minutes between 10am – 11 am for 06 months. The two Asian Indian male HES patients (Fig 3: H3, Fig 4: H4) were recommended simultaneous treatment of skin pigmentless patches topically with the defined protocol: the repeated massage with 5% w/w ethanolic extract of root powder of *Plumbago zeylanica* L. and orally with the intake of dose of 2g of root powder of the same plant twice a day with milk or water, followed by the exposure of relentless sun high intensity UVB daily for 07 minutes between 10am – to 11 am for 06 months.

RESULTS

The JQRMH analysis data (Table 1) have been revealing in regard to five markers: Phe, vitamin K, intestinal bacteria index, skin melanolipoprotein index and trace elements Cu^{2+} and Zn^{2+} with leads on their threshold limits in *Homo sapien* system, essentially required and defined under natural selection in defining skin pigmentary order. The factors which predispose conditions on the precipitation of skin depigmentary disorder or HES among the black Asian, African and Australian at tropics, have also been identified therefrom.

H6: Asian Indian generalised HES patient; H8 – h16: healthy normal Asian Indian with representative skin tone.

Normal range: Phe: 0.731 – 1.307; Vitamin K: 0.717 – 0.486; Intestinal bacteria index: 4.734 – 261;

Skin melanolipoprotein index: 0.346 – 0.501; trace element: Cu^{2+} and Zn^{2+}: 0.474 – 0.749 & 1.143 – 1.989.

Table 1: Complete Body Scan Analysis data on Asian Indian.

	Complete Body Scan Analysis Data					
Asain Indian Subject	**Phe**	**Vitamin K**	**Intestinal bacteria index**	**Skin melanolipoprotein index**	**Trace element**	
					Cu^{2+}	Zn^{2+}
H6	2.870	0.488	3.565	0.413	0.672	1.972
H8	2.944	0.560	3.242	1.297	0.575	2.717
H9	1.374	0.619	2.557	0.354	0.642	1.511
H10	1.987	0.560	3.242	1.297	0.575	1.415
H11	2.433	0.547	1.975	1.311	1.227	1.905
H12	2.229	0.550	2.178	0.973	1.325	2.122
H13	2.144	0.560	2.320	1.297	0.575	1.415
H14	2.804	0.490	3.941	1.294	0.534	2.354
H15	2.433	0.547	1.975	1.311	1.227	1.905
H16	3.419	0.541	2.887	1.691	0.554	1.327

The Asian Indian normal female put on the dose of 10g of Walnut Kernals (*Juglans regia* L.) twice a day for 12 months, followed by daily body exposure to relentless sun high intensity UVB for 07 minutes (between 10 am – 11 am), showed the signs of hyperpigmentation on the face and forehead (Fig 1 : H1).

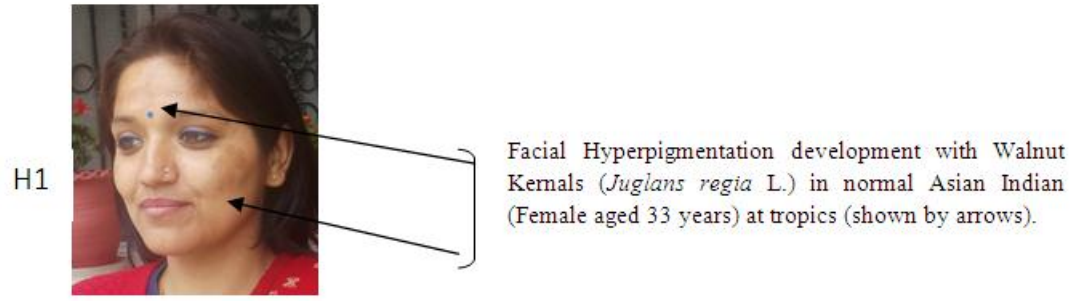

Fig. 1: Facial hyperpigmentation with daily intake of 10 g of Walnut Kernals (*Juglans regia L.)* twice a day by a normal female of 33 years for 12 months in sharp contrast to the surrounding hypopigmented areas.

The *Homo sapien* skin depigmemtary disorder or HES - a vitamin K deficiency disorder – has been rehabilitated with topical or simultaneous topical and oral treatment, defined under naphthoquinone therapy. The pigmentless skin of female HES patient on massaging into repeatedly for 06 months, followed by exposure to relentless sun high intensity UVB for 07 minutes daily with 5%w/w root extract of *Plumbago zeylanica* L in moisturizing cream resulted in 50% reduction in the initial size of the skin white patch (Fig 5: H5). In another male HES patient when treated with vitamin K_1 viscous liquid in combination with relentless sun high intensity UVB for 06 months, the untreated skin white patch shrank 75% (Fig 2: H2). In the other two male HES patients having white patches on the leg (Fig 3: H3) and skull (Fig 4: H4), when subjected to simultaneous treatment with 5% w/w root extract of *Plumbago zeylanica* L. topically and the dose of 2g of root powder of same plant twice a day orally, followed by daily exposure for 07 minutes between 10am – 11am of relentless sun high intensity UVB for 06 months, the complete disappearance of leg white patches (H3) was recorded whereas HES patient with small and medium size white patches on the skull showed about 75% recovery.

The concatenation of bioevents and intermediate dots, defined epidermaly under natural selection in *Homo sapien* system in the determination of skin pigmentary order with leads on pre – disposing factors of skin depigmentary disorder or HES among black *Homo sapiens:* Asian, African and Australian, and assumption of light – toned integumental coat by white European have been identified and decoded.

CASE 1

HsSDD or **HES Patient of Asian Indian origin (H2): age** 16years. **Repigmentary Response Period**; 06 months. **Treatment Mode**: Topical Treatment. **Test Drug**: Vitamin K_1 viscous liquid.

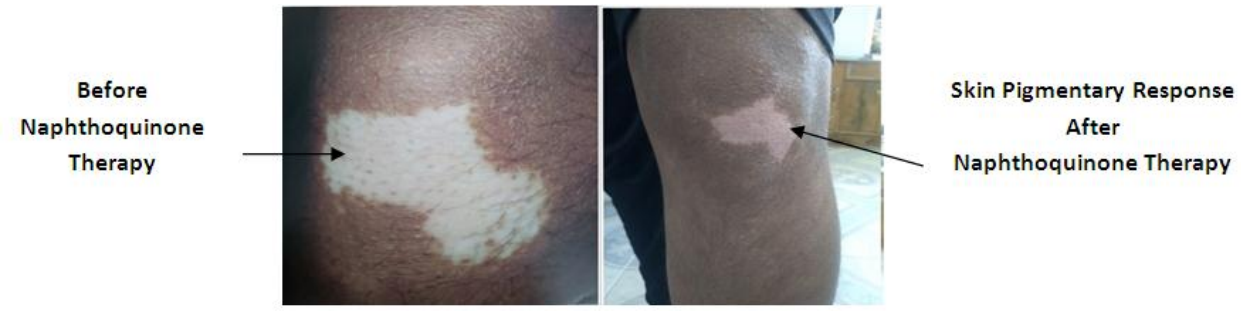

Fig. 2: Skin pigmentary response following treatment with topical massage of pigmentless skin patches with vitamin K_1 viscous liquid.

CASE 2
HsSDD or HES Patient of Asian Indian origin (H3): age 25years. **Repigmentary Response Period**; 06 months. **Treatment Mode**: Simultaneous Topical and Oral Treatment. **Test Drug**: Root powder of *Plumbago zeylanica* L

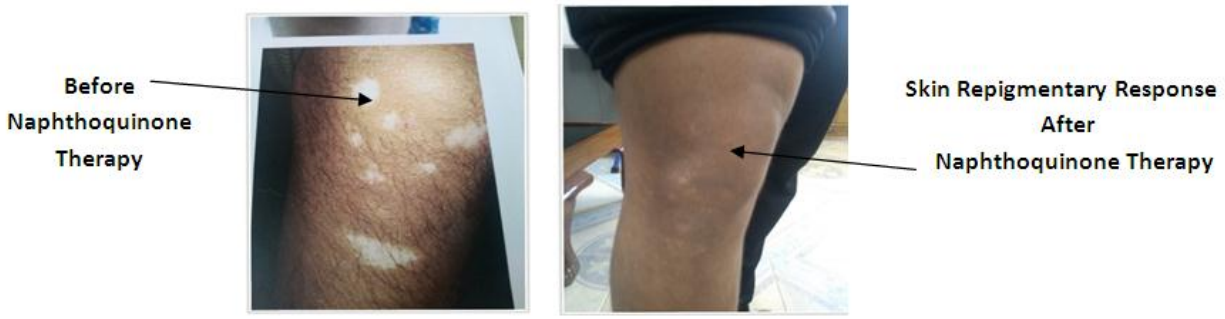

Fig. 3: Skin pigmentary response following treatment with topical massage of pigmentless skin patches with 5% w/w of root extract of *Plumbago zeylanica* L. in the moisturizing cream, and daily oral dose of 2 g twice a day of root powder of *Plumbago zeylanica* L. under naphhthoquinone therapy.

CASE 3
HsSDD or HES Patient of Asian Indian origin (H4): age 60years. **Repigmentary Response Period**; 06 months. **Treatment Mode**: Simultaneous Topical and Oral Treatment. **Test Drug**: Root powder of *Plumbago zeylanica* L.

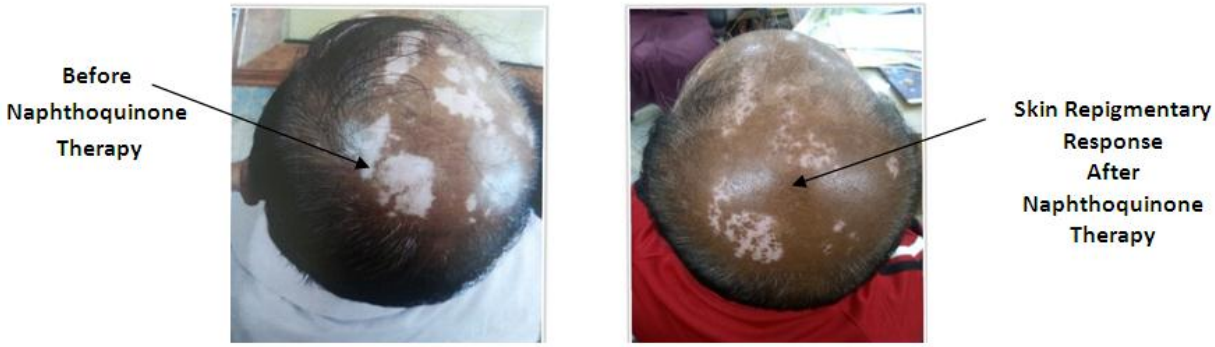

Fig. 4: Skin repigmentary response following treatment with topical treatment of pigmentless skin patches with 5% w/w root extract of *Plumbago zeylanica* L. in moisturizing cream, and daily oral dose of 2 g of root powder of *Plumbago zeylanica L.* for 06 months under naphthoquinone therapy.

CASE 4
HsSDD or HES Patient of Asian Indian origin (H5): age 25years. **Repigmentary Response Period**; 06 months. **Treatment Mode**: Topical. **Test Drug**: 5% w/w ethanolic extract of root powder of *Plumbago zeylanica* L in moisturising Cream.

Fig. 5: Skin repigmentary response following topical treatment of pigmentless skin patches with 5% w/w root extract of *Plumbago zeylanica* L. in moisturising cream.

Fig. 6: Some of the races of present *Homo sapiens* (aka present day humans).

H18. Tan Asian Indian, H19. Tan Chinese, H20. Tan American Indian. H21. Deep tan Australian aborigine, H22, Deep tan African.

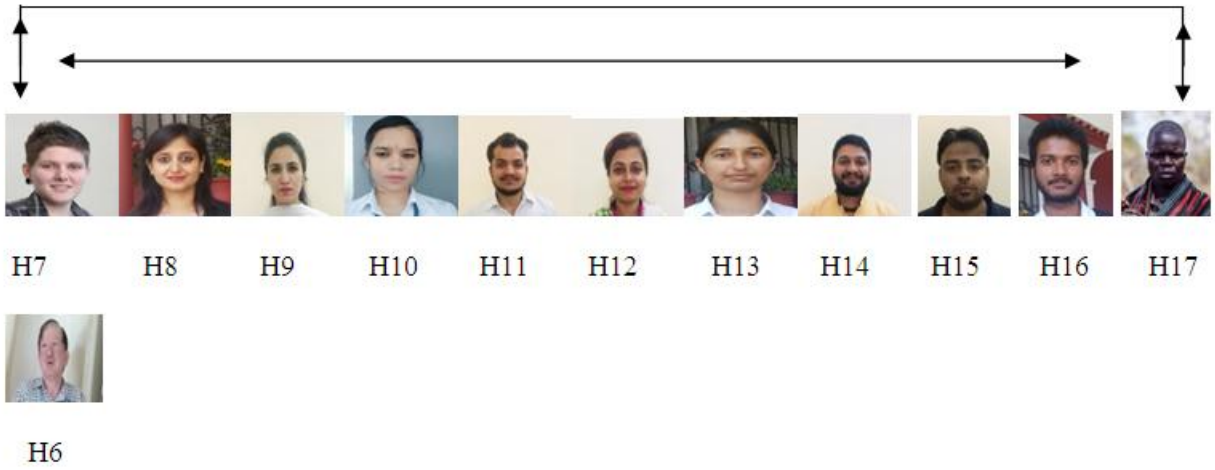

Fig. 7: *Homo sapien* skin-tone spectrum extremes. In between two extremes are shown the Asian Indian *Homo sapiens* at tropics with the representative skin-tones in the increasing order (left to right), H6. Asian Indian HES patient, H7. White European, H8. Asian Indian with sunless medium, H9. Asian Indian with sunless tan light, H10. Asian Indian with Causcarian light, H11, Asian Indian with moderately Tan, H12. Asian Indian with moderately Tan, H13. Asian Indian with Causcarian medium, H14. Asian Indian with moderately tan, H15. Asian Indian with moderately Tan, H16. Tan Asian Indian, H17. Deep black African.

DISCUSSION

The natural selection – centric blueprint upon black *Homo sapien* prototype upon earth defined with the continuum of epidermal facultative pigmentation over and above the pre – natal light – tined integumental coat at tropic – an incubatory for the evolution and conceptualization of *Homo sapien* in the context of relentless sun high intensity UVB had been defined, but with a code. The white European at beyond tropics and *Homo sapiens* with skin depigmentary disorder or HES condition at tropics are the defiances to the natural selection. The post – natal HES condition among black non – European or light – toned European skin is no disease per se, but an inversion to the pre – natal defined

light - toned integumental tone. The factors which cause skin depigmentary disorder among European at beyond tropics and non - European at tropics, are different. The skin depigmentary disorder is non - genetic in nature and reversible to the point of initially defined black *Homo sapien* prototype under natural selection. An Eurasian child, born to an Asiatic parent with skin - tone: moderate tan to dark tan and a white or European parent, shows the signs of intact epidermal system which defines skin pigmentary order on interplay with the relentless sun high intensity UVB at tropics. The epidermal pigmentary response on *Homo sapien* exposure to relentless sun high intensity UVB at peri- natal level is a defined normal under natural selection at tropics, but the *Homo sapiens* under normal body conditions fail to respond when subjected to relenting sun low intensity UVB at beyond tropics, suggesting the pivotal role of relentless sun high intensity UVB at tropics in defining and determination of skin pigmentary order which hedges the organal ecosystem defined under natural selection against the protein – denaturizing and cancer causing properties of UVR.

Black *Homo sapien* prototype, whose posterity being black modern humans at tropics (shown in Fig. 6: H18-H22), but not the white European at beyond tropics who are evolution defiances shown in Fig 7: H7, had been conceptualized and evolved, defining its earthly relevance under the sapient biostrategy of natural selection. The pre – natal gene -directing light - toned integumental coat as a wrap, showed the signs of earthy irrelevance with the defined vulnerability to skin cancer or cancer, ascribable to the free access of UVR beyond the epidermal and dermal limits, beyond which the organal ecosystem had been defined, causing irreversible denaturisation of the proteins, the organal ecosystem had been made of. This pre- natal imperfection in white *Homo sapien* model had been perfected to the point of its earthly relevance with the recalibration of the strategy under natural selection, defining its post – natal continuum of epidermal facultative pigmentation over and above the light- toned integumental coat with the inherent characteristics to resist the impacts of UVR at tropics upon earth. Melanolipoprotein- a conjugate of homopolymer indole- 5, 6- quinone (melanin) and lipoprotein, as defined by Sawhney[5], had been key to define continuum of epidermal facultative pigmentation which resists the impacts of UVR, reflecting and deflecting them, the moment the *Homo sapien* skin is impacted, but the concatenation of epidermal bioevents and the intermediate dots, which determine the *Homo sapien* skin pigmentary order, remain coded today, in spite of the best efforts invested into by the world scientists.

The demonstration of the skin pigmentary responses, registered by El Mofty,[8] applying the psoralens, the ingredients of *Ammi majus* L: Ammoidin (8-methoxypsoralen), Ammidin (8-amylinoxypsoralen) and Majudin (5- methoxypsoralen) in combination of relentless sun high intensity UVB, topically and orally upon the *Homo sapien* skin depigmentary disorder or HES subjects, had been revealing. The psoralens characteristically have been found highly photosensitive and UVB -harvesting. The corollary has been that the like biosignatures with high photosensitivity and UVB - harvestability had been the part of the strategy under natural selection to define the *Homo sapien* skin pigmentary order, given the eternality of relentless sun high intensity UVB upon earth, ascribable to the constancy and consistency of the ongoing radioactivity – driven fusion reactions upon the sun surface, showing no signs of degeneration over the billion years.

Closed examination of the chemistry of *Homo sapien* system at tropics revealed that the data on the biosignatures, which matter in a *Homo sapien* system, pointed to their poor to moderate photosensitivity and UVB - harvestability characteristics except the vitamin K – the family of vitamin K_1, an essential vitamer and K_2, the non-essential vitamer formed in vivo in intestinal track by the inherent intestinal microbiome from the flora- based naphthoquinone forerunners, which have been recognized as the highly photosensitive and UVB - harvester due to the inbuilt 1,4- benzoquinone chromophore (280- 320nm), showing comparable properties like those of psoralens. Secondly unequivocal role of vitamin K, defined with 2- methyl -1,4-naphthoquinone nucleus and fat solubility, in health is the maintenance of normal coagulation - a lifeline of *Homo sapien* system. The liver biosynthesizes vitamin K – dependent coagulation proteins called factors II, VII, IX and X, which have a haemostatic role i. e., they are procoagulants that arrest and prevent bleeding, and proteins C and S, which have anticoagulant role i.e., they inhibit the clotting process. Despite this duality of function, the over-riding effect of nutritional vitamin K deficiency is to tip the balance in coagulation toward a bleeding tendency. The other tissues biosynthesize bone protein osteocalcin and matrix Gla protein. The other wide applications of vitamin K in *Homo sapien* system have been registered. The vitamin K universality in *Homo sapien* system as defined under natural selection, is an established fact now, and has been the dependable guide with leads on the resolution of the previously unknown biomechanisms of *Homo sapien* skin pigmentary order and depigmentary disorder and its attendant skin cancer or cancer. Surprisingly its role in skin organ has been missed out so far.

As a corollary, it has been hypothesized that the vitamin K had been the signature biosignatures, defined under natural selection in defining *Homo sapien* skin pigmentary order in combination with the relentless sun high intensity UVB with leads on the aetiology of *Homo sapien* skin depigmentary disorder (HsSDD) or HES and its attendant skin cancer (HsSC) or cancer (HsC) and their treatment and prevention. The strong responses of vitamin K to high intensity UVB, agreeably true to the relentless sun high intensity UVB, validated the defined

preference under natural selection, of tropics as the defined incubatory upon earth to conceptualize and evolve black *Homo sapien* prototype.

The hyperpigmentation as recorded in the case of normal Asian Indian with Walnut Kernals (*Juglans regia* L) (Fig 1: H 1) validated the vitamin K hypothesis as the major ingredient of Walnut Kernals : juglone : 5- hydroxy-1, 4-naphthoquinone gets biotransformed to vitamin K_2 in intestinal track through the action of inherent intestinal microbiome, resulting in the rise of vitamin K level in the epidermis, followed by excessive intramelanocytical biosynthesis of melanolipoptrotein and its subsequent layer to layer migration to stratum granulosum – the defining layer of skin pigmentary order, given the eternality of relentless sun high intensity UVB at tropics, which on interplaying with the epidermally defined vitamin K releases offspring photon energy – a pivotal force in defining skin pigmentary order. The repigmentary response in HES patient: H2 – H5 either with the topical application of vitamin K_1 viscous liquid or 5% w/w root extract of *Plumbago zeylanica* L. or simultaneous topical and oral application of 5% w/w extract of *Plumbago zeylanica* L and 2g dose of root powder of the same plant in combination with the relentless sun high intensity UVB for 06 months also validated vitamin K hypothesis on the exploitation of vitamin K (a group of vitamin K_1 and K_2) as the pivotal biosignatures as defined under natural selection in the determination of *Homo sapien* skin pigmentary order, as the principal ingredient of *Plumbago zeylanica* L: plumbagin, 5 – hydroxy- 2- methyl – 1, 4 – naphthoquinone is biotransitioned to vitamin K_2 (MK –n where n = 2 -12) through the action of intestinal microbiome.

The basic principle of photochemistry had been exploited under natural selection in the determination of skin pigmentary order in order to help black *Homo sapien* prototype or its posterity (black modern humans) stay sustained and adapted at tropics upon earth. Secondly, the geometrically defined tendency of vitamin K, defined with the inbuilt 1,4- benzoquinone chromophore, to high intensity UVB at tropics, had been revealing on leads on the biomechnism of skin pigmentary order under the bioscheme of natural selection. The epidermally defined vitamin K threshold volume defined with the inherent tendency to photoreact the high intensity UVB only, could harvest, interplay the relentless sun high intensity UVB at tropics undergoing itself dimerization, following photochemical [2+2] cycloaddition involving HOMO – LUMO interaction with the release of offspring photon energy which has been identified and decoded as the key force in defining *Homo sapien* skin pigmentary order at tropics among the black *Homo sapiens (*Asian, African and Australian)as shown in Fig. 8. The singlet to triplet excitation transition (Fig.9) shows that the vitamin K harvests UVB first and gets excited to singlet state (S_1) from the ground state (S_0), and then passes to stable triplet state (T_1) via inter system crossing (ISC), releasing photon energy to be utilized in the intramelanocytically defined centres for the melanolipoprotein biosynthesis and the energisation of the inherent skin migratory mechanism to effect effectively the layer to layer melanolipoprotein migration to stratum granulosum – the defining epidermal layer of *Homo sapien* skin pigmentary order.

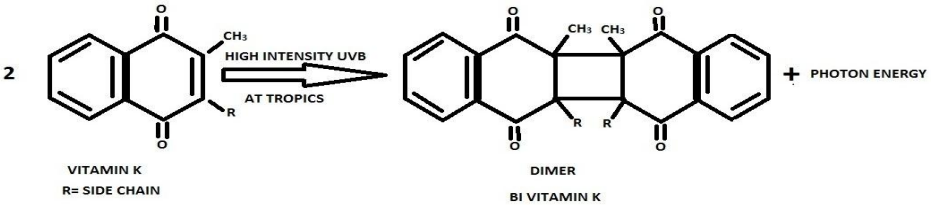

Fig. 8: Vitamin K dimerization under the influence of high intensity UVB at tropics.

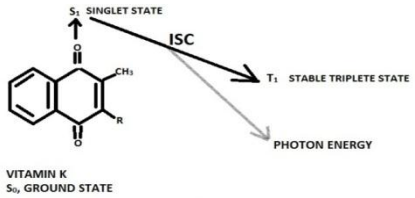

Fig. 9: Singlet – triplet excitation scheme.

The concatenation of epidermal bioevents and intermediate dots, which had been defined under natural selection in defining *Homo sapien* skin pigmentary order, have been identified and decoded. The defined determinants included: four pre-natal determinants: 1) Intestinal Microbiome 2) Light-toned Integument – based Vitamin K Threshold 3) Intramelanocytical Dormancy- centric Molecular Environment, composing of tyrosine, tyrosinase, lipoprotein, O_2, Cu^{2+}, Zn^{2+} 4) Skin Dormancy- centric mechanical migratory mechanism, and four post-natal determinants: 5) Tropics 6) Relentless Sun high intensity UVB 7) Flora- based Vitamin K_1 and naphthoquinones as precursors to Vitamin K_2 8) Trace Elemental: (Cu^{2+}, Zn^{2+}) Blood Threshold.

The activities of 1,2,5,6,7,8 determinants have been identified, but the determinants 3, 4 showed signs of molecular and mechanical dormancy at peri-natal level in *Homo sapien* system at tropics. The molecular and mechanical dormancy breach has been identified as the key to the determination of *Homo sapien* skin pigmentary order, given the defined bioactivities of the other determinants. The mere exposure of the pre- natal gene- directing light- toned integumental coat to relentless sun high intensity UVB could neither break the defined dormancy nor elicit skin pigmentary response. It had been demonstrated as referred earlier (Figs. 8,9) that it had been the offspring photon energy, the resultant of the union and interplay of the defined vitamin K threshold level in the epidermis and relentless sun high intensity UVB, which had the inherent potential to break intramelanocytical molecular dormancy and epidermal mechanical migratory dormancy, and initiate the epidermally defined bioprocess leading to *Homo sapien* skin pigmentary order. The offspring photon energy with its transduction to intramelanocytical centres, triggers the translation of tyrosine enzymatically and oxygenically to melanolipoprotein involving trace elements: Cu^{2+}, Zn^{2+}, following the steps as proposed by Fitzpatrick[33] et al. The melanolipoprotein transfer follows dendritically from the melanocytes to stratum basale to its fill, from where its further migration takes place to the next contiguous stratum spinosum, and then to the next contiguous stratum granulosum- the defining epidermal layer of *Homo sapien* skin pigmentary order, with the offspring photon energy- driven epidermal mechanical migratory mechanism. This epidermal endowment had been defined optionally under natural selection, but its lasting character had been biostrategised under natural selection with staying cyclic course of epidermal bioevents leading to the skin pigmentary order. The inferences drawn with leads on the course of epidermal bioevents to the point of stratum granulosum pigmentation, have found validation in the Complete Body Scan Analysis, carried out on the Asian Indian subjects:H6, H8 – H16 (Table 1).

The data (Table 1) on H6, H8 –H16 Asian Indian subjects showed that *Homo sapien* Phe levels did not fall below its threshold as the registered JQRMH values had been higher than the upper limit of normal range 0.731 - 1.307 except H10 which followed the normal range. The trace elemental data on Cu^{2+}, Zn^{2+} registered by these Asian Indian subjects either fell within the normal range: Cu^{2+} normal range: 0.474 – 0.749 and Zn^{2+} normal range: 1.143 -1.989 or assumed higher JQRMH values than the upper limits of Cu^{2+}, Zn^{2+} normal range. The Phe threshold normality in *Homo sapiens* led to the tyrosine threshold normality as Phe is the forerunner to tyrosine in vivo. The intestinal bacteria coefficient data on H6 registered was 3.565, being far higher than the upper limit of its normal range: 1.734 – 2.621. H9, H11, H12, H13, H15 registered values followed the normal range whereas the values on H8, H10, H14,H16 crossed the upper limit of normal range, suggesting the intactness of intestinal microbiome responsible for the biotransformation of the flora – based naphthoquinone forerunners to vitamin K_2. The H6 recorded vitamin K values as 0.488 - 0.002 unit higher than the lower limit of normal range: 0.717 -0.486 whereas the other Asian Indian subjects with the representative skin - tones assumed higher value than H6 and lower limit of the normal range. The data further revealed the lowest value of vitamin K in H6 among the Asian Indian subjects studied suggesting that the vitamin K low levels in the *Homo sapien* system has been the precipitating factor of *Homo sapien* skin depigmentary disorder among the black Asian, African and Australian races. Secondly the vitamin K could be the pivotal biomolecule, defined under *Homo sapien* evolutionary bioscheme in the determination of *Homo sapien* skin pigmentary order. The H6 (HES subject) and H9 with sunless tan light skin - tone displayed skin melanin index (= skin melanolipoprotein index) values as 0.413 and 0.354 respectively which had been slightly higher than the lower limit of normal range: 0.346- 0.501 whereas other Asian Indian subjects registered data far higher than the upper limit of normal range. The examination of the values revealed that H6 had far lower values as compared to H8 – H16 Asian Indian subjects, suggesting a clear corelationship between vitamin K and the epidermal melanolipoprotein volumes or the *Homo sapien* skin pigmentary order. The vitamin K data had been suggestive of the facts too that the vitamin K volume in *Homo sapien system* never fell below the normal limit of normal range. The vitamin K level in the *Homo sapien* skin depigmentary disorder or HES subject (H6), equivalent to the vitamin K value: 0.488, nearly equivalent to the lower limit of its normal range, has been concluded as the minimal organal bio-needs of *Homo sapien* system except the skin organ, failing relentless sun high intensity UVB to photoreact with the vitamin K and produce enough offspring photon energy to define *Homo sapien* skin pigmentary order. The higher vitamin K values as registered by H8- H16: 0.490 – 0.619 and their comparison to H6 values: 0.488 suggested on calculation the median vitamin K value of its normal range (approximately 25% higher than the lower limit of normal range) as the standard epidermal vitamin K threshold volume for photoreaction and interplay with the relentless sun high intensity UVB to release enough offspring photon energy to define skin pigmentary order.

The preceding discussion on the subject in reference has been revealing on the codes defined under natural selection thereon. First, the tropics as the incubatory for the conceptualization and evolution of black *Homo sapien* prototype had the scientific basis. The vitamin K as central and seminal force in defining *Homo sapien* skin pigmentary order, has been found with an inherent tendency to harvest high intensity UVB only which had been the guiding factor for clinching tropics, defined with suitable climatic conditions including relentless sun high intensity UVB, as an incubatory for *Homo sapien*

conceptualization. Second, given the demonstrated incapability of the individual player: epidermal vitamin K threshold or relentless sun high intensity UVB, to elicit skin pigmentary order, the epidermally defined union and interplay of vitamin K with its complementary relentless sun high intensity UVB, had been exploited and biostrategised under natural selection to define the skin pigmentary order at tropics. Third, the defined continuum of epidermal facultative pigmentation over and above the pre- natal light- toned integumental coat had been the defined epidermal hedge against the access of UVR beyond the epidermal and dermal limits, beyond which the organal ecosystem had been defined under natural selection – a defined epidermal endowment for sustaining the organal naturization permanently. Forth, the identification and decoding of factors, which define *Homo sapien* pigmentary order, have given the decisive leads on the aetiology of *Homo sapien* skin depigmentary disorder or HES and its attendant skin cancer or cancer and the mode of their treatment and prevention. Fifth, the genes, which directed the pre – natal protein- based organal ecosystem with light - toned integumental coat as wrap, defined as white *Homo sapien* model, had performed or continues to perform effectively with no geographical bar whatsoever upon earth. Sixth, UVB – resistant melanolipoprotein - centric skin pigmentary cover thereon the pre – natal light - toned integumental endowment had been the necessity and compulsion of human evolution. Seventh, the epidermal vitamin K levels of *Homo sapien* system need to be sustained quite higher than the minimal organal bioneeds with the daily judicious intake of flora – based vitamin K_1 and naphthoquinone fore- runners to vitamin K_2 in addition to *Homo sapien* staple diet, to contain *Homo sapien* skin depigmentary disorder or HES among the black non-European, Asian, African and Australian etc. and skin cancer or cancer among white European. Eighth, the skin cancer or cancer has been termed as the result of the denaturisation of the proteins, made under DNAbases instructions in vivo, the *Homo sapien* model is made of. Ninth, the vitamin K has been identified and decoded as a natural answer to skin cancer or cancer and skin depigmentary disorder or HES. Tenth, the representative skin - tones assumed by *Homo sapiens* at tropics (Fig.7: H8 – H16) have been attributed to the individual to individual variation in the relentless sun high intensity UVB exposure, given the defined epidermal vitamin K threshold volume. The dark black skin - tone of *Homo sapien* prototype as seen in its posterity like dark black African (Fig.6: H22) had or has been the attribute of the maximal body exposure to the relentless sun at tropics. Eleventh, the alarming increase in skin depigmentary disorder or HES among the black Asian, African and Australian etc. at tropics and skin cancer or cancer among white European and black non - Europeans at tropics and beyond has been registered and attributed to the modern humans' divorce from the flora – based staple diet in the modern era, in sharp contrast to the early humans who remain fully tuned to nature and lived disease - free lives upon earth.

Given the eternality of relentless sun high intensity UVR at tropics, the *Homo sapien* skin depigmentary disorder or HES has been identified as a vitamin K deficiency disorder among the black Asian, African and Australian etc., whereas the *Homo sapiens* (white European) inhabitating beyond tropics had assumed light - toned integumental coat- a skin depigmentary disorder, ascribed to the relenting sun low energy UVB which failed to photoreact the epidermal vitamin K levels.

The peri – natal advent of *Homo sapien* life upon earth with quite empty epidermal layers sans melanolipoprotein traces, had been 100% vulnerable to UVR to the point of denaturisation of organal ecosystem – the sign of trigger of skin cancer or cancer. The biostrategic lining of the epidermal layers: stratum granulosum, stratum spinosum and stratum basale with melanolipoprotein to the defined degree, had helped *Homo sapien*s stay sustained and adapted upon the earth with the resulting epidermal lines of defences against UVR, coined as ESGLD (first defence line), ESSLD (second defence line) and ESBLD (third defence line). The epidermal pigmentation upon stratum granulosun at tropics had been purely facultative (optional) as defined under natural selection and continues departing from its surface to be removed by desquamation. The challenge had been met under natural selection with the maintenance of constancy and consistency of the epidermaly defined vitamin K threshold volume, given the constant character of relentless sun high intensity UVB, to sustain the lasting character of melanolipoprotein density in stratum granulosum – the defining layer of *Homo sapien* skin pigmentary order. The *Homo sapien* life with acquired skin depigmentary disorder or HES at tropics (HES subjects) and beyond (White European), loses first line of defence (ESGLD) only, but resists UVR and skin cancer or cancer with the other unaffected lines of defences: ESSLD and ESBLD. The white Europeans at beyond tropics with the declining epidermal vitamin K volume to the minimal level would assume maximal vulnerability to skin cancer or cancer, and need to be protected with the regular intake of flora – based vitamin K_1 and naphthoquinone fore – runners to vitamin K_2.

The *Homo sapien* skin depigmentary disorder or HES and skin cancer or cancer are now containable with the maintenance of the epidermal vitamin K threshold volume, quite higher than what is biorequired for the organal ecosystem. It has been made possible with Naphthoquinone Therapy developed here which offers new and effective options for the treatment, prevention and pre-emption of skin depigmentary disorder and skin cancer or cancer with the redefining of the epidermal vitamin K levels to the defined point with the oral administration of the root powder of *Plumbago zeylanica* L, defined with plumbagin (5- hydroxy-2-methyl-1,4-naphthoquinone) as the main ingredient, biotransformable to vitamin K_2 in vivo in intestinal track with the intestinal microbiome action thereon.

To keep at bay permanently the skin depigmentary disorder or HES and skin cancer or cancer, the *Homo sapiens*, spread over the whole earth at tropics and beyond (white European at beyond tropics) and HES subjects and black non-European Asian, African and Australian etc. at tropics) are recommended to supplement their staple diet with the daily dose of 10g of Walnut Kernels (*Juglans regia* L.) and 2g root powder or its equivalent extract of *Plumbago zeylanica* L. – the ingredients of which: juglone (5- hydroxy-1,4-naphthoquinone) and plumbagin (5- hydroxy-2-methyl-1,4- naphthoquinone) respectively, are biotransformed in intestinal track with the inherent intestinal microbiome to vitamin K_2 or any other flora – based vitamin K_1 or naphthoquinone fore- runners to vitamin K_2 sources.

CONCLUSION

The vitamin K has been identified as the pro skin pigmentary order, anti-skin depigmentary disorder and anti-cancer vitamer. The supplementation of staple diet with plant -based highly photosensitive and UVB-harvesting 1, 4-naphthoquinone derivatives: root powder of *Plumbago zeylanica* L and fruits of *Juglona regia* L, is strongly recommended to keep skin depigmentary disorder and cancer at bay.

REFERENCES

1. Van den Wijngaard, RM, Scheepmaker AJ. Expression and modulation of apoptosis regulatory molecules in human melanocytes: significance in vitiligo. Br J Dermatol, 2000; 143(3): 573- 81.
2. Spritz RA. The genetics of generalized vitiligo. Curr Dir Autoimmu, 2008; 10: 244 – 257.
3. Sravani PV, Babu NK, Gopal KV, Rao GR, Moorthy B. Determination of oxidative stress in vitiligo by measuring superoxide dismutase and catalase levels in vitiliginous and non - vitiliginous skin. Ind J Dermatol venerol leprol, 2009; 75(3): 268 -270.
4. Kovacs SO. Vitiligo. J Am Acad Dematol, 1998; 38: 647 – 66.
5. Sawhney SS. Thermal stability of melanin. Thermochim Acta, 1994; 247: 377 – 380.
6. Sawhney SS. Genesis of cutaneous depigmentation. Ind J dermatol venerol laprol, 1996; 62: 200 – 201.
7. Sawhney SS. Aetiology and treatment of epidermal depigmentary disorder in humans. Nature Proceedings ≤http:hdl.handle.net/10101/npre, 2012; 7025 - 17.
8. Mofty El AM. Further study on treatment of leucoderma with Ammi majus L. J Egypt med Ass, 1953; 35: 1.
9. Taketsugu T, Yugi Y, Jan B, Sergio GC, Barbara JJ, Sharonm AM, Rainer W, Junusz ZB, Vincent JH. Mechanisms of skin tanning in different racial/ ethnic groups in response to ultraviolet radiation. Invest Dermatol, 2005; 124: 1326 – 1332.
10. Preston DS, Stern RS. Nonmelanoma cancers of skin. N Eng J med, 1992; 327: 1649 – 1662.
11. Kricker A, Armstrong BK. Sun exposer and skin melanocytic skin colure. Cancer Causes & Control, 1994; 5: 367-392.
12. Halder RM, Bridgeman S. Skin cancer in African Americans. Cancer, 1995; 75: 667-673.
13. Xiao K, Zardawi FM, Yates JM, Sueeprasan S. Characterizing the variation in ethnic skin colures: a new calibrated database for human skin. Skin Res Technol, 2016; 23(1): 21-29.
14. Madison KC. Barrier function of the skin: "la raison d'etre" of the epidermis. J Invest Dermatol, 2003; 121(2): 231- 241.
15. Rees JL. Genetics of hair and skin colour. Annu rev gene, 2003; 37: 67-90.
16. Kollias N. The physical basis of skin colour and its evaluation. Clin Dermatol, 1995; 13: 361-367.
17. Meredith P, Sarna T. The physical and chemical properties of eumelanin. Pigment cell res, 2006; 19: 574-594.
18. Alison MD, Richard JP, Mark EH, Andrew DA. The synthesis of naturally occurring vitamin K and vitamin analogues. Curr Org Chem, 2003; 7: 1-15.
19. Datta S, Mishra RN. Plumbago zeylanica L – review as rasayan (rejuvenator/ anti-aging). J Pharm Biomed Sci, 2012; 3(1): 250 – 266.
20. Sawhney SS. 2 - Hydroxy -1, 4 - naphthalenedione (lawsone) a pH indicator. J Indian Chem Soc, 1977; 4: 641.
21. Sawhney SS, Trehan N C. 5- Hydroxy - 1, 4-naphthoquinone (juglone) a new indicator in acidimetry & alkalimetry. Indian J Chem, 1976; 14A: 295-296.
22. Sawhney SS, Vohra N. 2-Hydroxy-3-(3-methyl- 2-bytenyl)-1, 4- naphthoqunone (lapachol) - a new pH indicator. J Indian Chem Soc, 1977; 54: 403-404.
23. Sawhney SS, Bhatia BML. Analytical application of 5- hydroxy-1,4- naphthoquinone (juglone). J Indian Chem Soc, 1984; 57: 438-439.
24. Sawhney SS, Matta SD. pH- metric, spectral, magnetic and thermal investigation of Ni - 2-hydroxy– 3 - (3 – methyl – 2 - butenyl) - 1, 4 - naphthoquinone (lapachol) complex. J Indian Chem Soc, 1980; 57: 497 – 499.
25. Sawhney SS. Studies of the inner salt complex of 2-hydroxy- 1, 4- naphthoquinone (lawsone) with Hg (II). Thermochim Acta, 1984; 74: 361- 364.
26. Sawhney SS, Jain R. The Gd (III), Th (IV) affinity of functional groups in hydroxy - naphthoquinones. Thermochim Acta, 1986; 98: 391- 394.
27. Sawhney SS, Sati RM. Kinetics and x-ray powder diffraction studies on dehydrated bis (2 – hydroxy-1, 4 -naphthoquinone) Cobalt (II) and Nikel (II) complexes. Thermochim Acta, 1987; 115: 385-387.
28. Sawhney SS, Arora NK. Equilibrium analysis of La (III) – and Pr (II) – 3- methyl – 5-hydroxy-1, 4-naphthoquinone systems. Thermochim Acta, 1987; 115: 385 – 387.
29. Sawhney SS, Sati RM, Chandel SK. Kinetic analysis of derivative thermogravimetric data of 5-hydroxy - 1, 4- naphthoquinone (juglone) and some of its

divalent metal chelates. Thermochim Acta, 1982; 55: 363-365.
30. Sawhney SS, Bains SS, Bisht DS. Investigation on UO^{2+} - 2 - methyl- 5- hydroxy-1, 4- naphthoquinone complex. Thermochim Acta, 1983; 67: 107-109.
31. Sawhney SS, Vohra N, Chandel SK. Formation constants and thermodynamics functions of Cd (II), Zn (II), Pb (II), VO^{2+} and Ce (IV) with lapachol. Thermochim Acta, 1982; 52: 349-350.
32. Sawhney SS, Matta SD, Jain R, Kasyap RK, Painuli VK. Investigation on interaction of 2-hydroxy-3- (3-methyl-2-butyl)-1, 4-naphthoquinone) (lapachol) with Co (II) and Fe (II). Thermochim Acta, 1983; 70: 367-371.
33. Fitzpatrick TB. Tyrosinase in human skin: demonstration of its presence and its role in melanin formation. Science, 1950; 112: 223.