



## **Transmission Blocking of Year Round Resistant Malaria in Koraput (India) by OMARIA – A New Antimalarial Phytotherapy**

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### **Authors' contributions**

*This work was carried out in collaboration between all the authors. Author DB designed the study, performed statistical analysis, literature searches, wrote the protocol, did analysis and the first draft manuscript. Author BMB provided Govt. records & field support, author PKP lead clinical works, author DKN provided geo-spatial aspects. All authors read and approved the final manuscript.*

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### **ABSTRACT**

**Background:** Globally, in resistant malaria endemic zones, even the latest lines of MDTs (multi drug therapies) are yielding chaotic results. These include unacceptable side effects/contraindications, with poor prognosis in juveniles/adolescents. Juvenile stage is intensely humoral and up-regulate infestation. MDTs are more unpredictable in the juveniles, and fail in the geriatric group. Pharmacies are also failing. Tropical-equatorial conditions necessitate frugal body cover cum bare foot life style. Typical geomorphology, orography, meteorology, flora and fauna provide year round conducive conditions for vector bionomics and for other types of infections. OMARIA (Orissa Malaria Research Indigenous Attempt) is a new anti-malaria phytotherapy that has been in mono station use (Koraput, India) since 1998 in drug resistant core endemic regions, also well known for tertian type. It transpired out of Koraput Model to Fight Malaria at Home with OMARIA.

**Materials and Methods:** OMARIA is composed of the dry rind of the Indo-year round fruiting *Punica granatum* (Dalimba). Principal drug moieties are: (i) ellagic acid; (ii)

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punicalagin (iii) punicalin and (iv) potassium ( $K^+$ ). Are physiologically compatible and has never been used before. All the moieties being non alkaloids offer a paradigm shift among anti-malarials.

**Results:** OMARIA kills and clears hemoprotozoas of all spp., at all stages (including gametocytes) in patients of all ages and chronicity. Is potently anti-inflammatory vis-a-vis WBCs; blocks transmission; prevents relapse and non- recrudescence; and is very useful in severe/acute/complicated/refractory malaria and in sickle cell patients. No development of resistance. Potassium ( $K^+$ ) probably acts as the drug's efficacy upregulator.

**Conclusion:** OMARIA is prophylactic and therapeutic in target groups. Is useful in numerous forms of malaria, being active against key stages of the parasite (complicated or systemic status); and in patients having multiple infections. It has synergistic and possibly buffering roles. Koraput Model has been of much help to the afflicted communities and to the administrations.

*Keywords: Transmission block; OMARIA; Dalimba (Punica granatum); geriatric; juvenile/adolescent; menopause; poly infections; prophylactic; therapeutic; Koraput model; fight malaria at home.*

## 1. INTRODUCTION

Mr. Mohandass Karamchand Gandhi, the immortal Father, of the lovely Indian nation (educated as a Barrister at London) in his days of yeoman leadership, had staunchly preferred herbal medicine, to the exception of all [1]. All over India, numerous *in-memorium* plaques in erstwhile European cemetery announce the demise within 1yr of landing, having fallen to malaria. During the same historical period, due the absence of robust-(regional)-erudite classical school(s) of herbalism (as alike Ayurveda) the West Africa region got to be called as the "white man's grave" [2]. World-wide, herbalism is being focused upon as profitable source in drug discovery [2]. In India, there seems to be a non-complementing relationship between the allopathic clinicians and others [3]. The USMLE (United States Medical Education Licentiate Examination) requires the Indian MBBS and the MD degree holders to go through a 3 step examination, termed Step 1, Step 2CK (clinical knowledge), and Step 2CS (clinical skills) which is said to take years [4]. And, the native wherewithal of India the land of Ayurveda (intonated as Aayoor-Veda alias plural health) and related historical evidences (Bhattacharya, 2009) have largely remained un-explored by multi-lateral initiatives. Unfortunately, the Indian allopaths are discouraged from prescribing and/or adopting herbalism/Ayurveda (incalculable national loss and is also counter to Indian national ethos). The Hindu (unshakable of faith) also is fiercely possessive; awesomely conservative and has mastered the technique of - hide and deny. Amidst such conditions, we have tried to remain focused on the ground to produce the 15yr long on-foot social service based field observations as abstracts[5-9] from the remote of rural India (Koraput; 18°49'N/82°43'E).

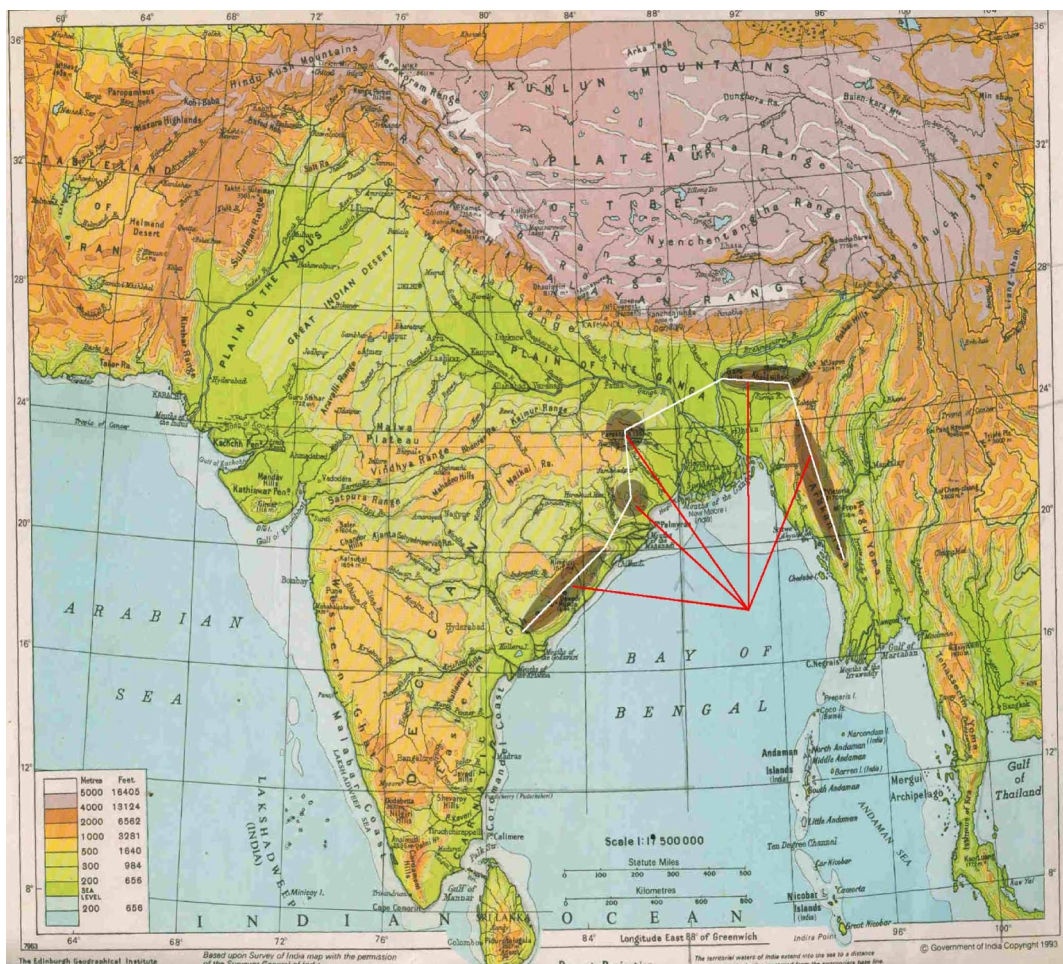
Outside India, not much is known about the Indian effort story; the triumphs and the failures *vis-à-vis* malaria combat. The National Malaria Control Program [10] and the National Malaria Eradication Program [11] were launched in 1953 and 1985 respectively and were evaluated by the Govt. of India [12]. During the present decade, the National Rural Health Mission [13] has been launched. It also has malaria combat and our domain as focus region as its objectives. However, it does not patronize modern herbalism and/or Ayurveda as much as it does to allopathic.

Even then, the national and/or the sectoral malaria graphs have remained obstinate, with domain enlargement in resistance to CQ (chloroquin). The ACTs (arteimisinin combination therapies) are randomly used in more than  $\frac{1}{2}$  of the Indian geography [14]. So also is the emergence of new and more resistant mutant strains [15], that are ACT and MDT (multi/mixed drug therapy) resistant and also offer variable drug susceptibility. The ACTs and other MDTs collinearly also offer variable toxicity and inflammation. The Indo national financial layout to combat malaria is not large enough as compared to the size of the task (India is a subcontinent with a Billion<sup>+</sup> populations of various stocks and cultural practices). The present focus has also gravitated away from that of the objectives of the India National 5 yr., Plans (Ayurveda → modern herbalism). Nevertheless, she has done well.

India also has few mini anti-malaria operations, one of which is called 'Fight Malaria at Home' (FMH) alias *Ghare Maro Malaria*. It is a part of the Koraput Model (herbalism). It uses a natively invented and indigenously made drug called 'OMARIA'-Orissa Malaria Research Indigenous Attempt-(is one part, apart others), about which very little is known even within India [16]. Globally, malaria is endemic all over the tropo-equatorial domains limited to 2000meters from the MSL (mean sea level). The geography and the census of the OMARIA use domain (Koraput district, eastern shore board of India) is a plateau of the order 750-1000mts above the MSL, with a geographical area of 100,000Km<sup>2</sup> and a census of 1million; 65-70% of which are non migrating, native tribal of ethnic stock. The epidemiology status of this region is well known being variously documented [17]. In 1989 (implementation yr. of FMH) Rajagopalan et al. [18] have indicated that even pediatric stage malaria to be high in Koraput. Infestation in all age groups is round the year. OMARIA use in Koraput commenced from 06-1998 (it is now preferred). The natives have a frugal body cover cum bare feet life style. This is because of the (i) agro – flora couple (ii) geomorphology (iii) meteorology which includes the land-atmosphere and the sea-land couples. Which in turn because a robust transmission mechanism aided and abetted by another unique couple involving (iv) the asymptomatic gametocyte carriers {also exhibit high drug resistance} and vector bionomics cum aerodynamics (v) poly infestation and/or poly infections along-with malaria.

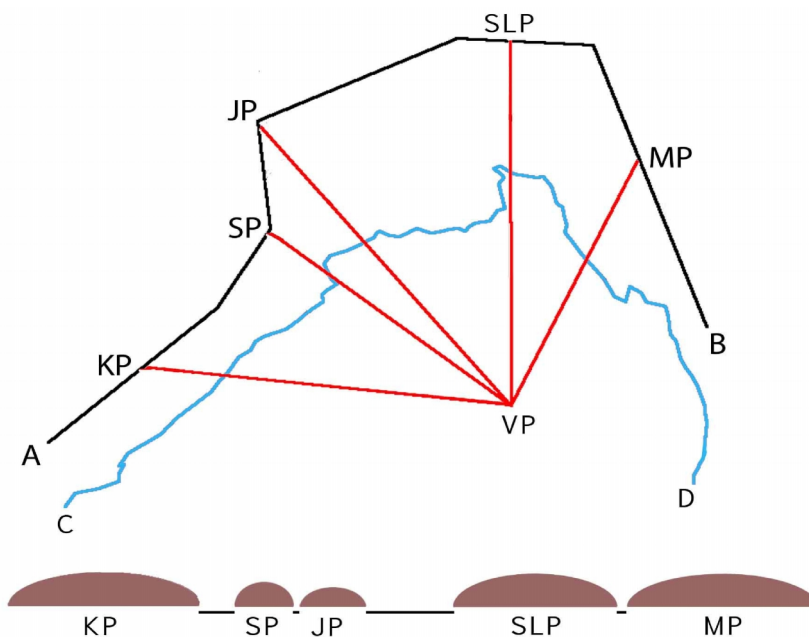
Accounting from the Koraput cum Kandhamal (kp); Similipal (slp); Jharkhand (jp); Shillong (slp) and Mezo-Manipur (mp) are 5 plateaus that encircle the warm apex region of the triangular Bay of Bengal (BoB, Fig. 1), with lush-green inter-plains in-between. Geologically the slp and the mp are of Eocene period, the rest are of Gondwana. Excepting the slp the other plateaus are oblique to the lines of the sea-atmosphere forcings (slp is also >3000mts.above MSL). Fig. 2 gives a schematic frontal elevation from view position (vp) located in mid BoB, when A-B is drawn straight. Locus vp and the forcings are meteorologically significant. Line C-D represents the shore line. Thus the plateaus have variable extents of coastal land as apron, which are historically over populous; lush green; low lying, with land↔sea breeze (excellent buffer cum hibernating domain). Line A-B hypothetically also marks the vector-parasite conducive year round land↔sea breeze region and also demarcates the coastal region that is low lying, cramped with natural seasonally stagnant water bodies and is intently malaria prone. Diurnally, the tropical foliage loaded plateau synclines experience a salubrious up-draft in the fore-noon hours and a cool-moist down draft, post noon. Annual atmospheric moisture remains consistently high with gain in astronomical gravity during full moon phases, which in turn imparts buoyancy to the vectors. Due size-mass barrier, gravity plays not on the hemoprotozoa (weightless). This assists the vectors to communicate large distances and remain ever in circulation. Between these lush green, tropical coastal plateaus and the populous, moist plains around, the infested vectors fly in-and-out, year round. Such geography is unique. Hence, vector control efforts have all

come naught and, OMARIA is the fresh new drug candidate (source) in long term use in the kp-sp axis.

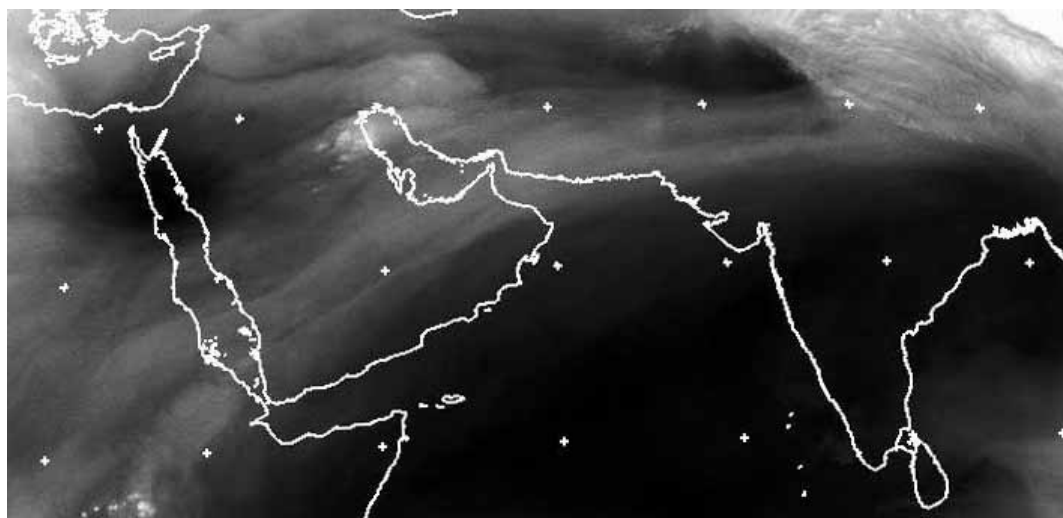


**Fig. 1. The eastern shore board of the Indian peninsula showing 5 major plateaus that encircle the warm apex region of the Bay of Bengal, that also experiences year round forcings of the sea-atmosphere couple. Choice domain for vectors bionomics.**

Drug resistant strains differ between Asia and Africa. On the other hand, robust atmospheric tele-connection pathways exist between Africa and Asia, due to the geostrophic rotation of the Earth; its inclination and baroclinic conditions (planetary scale). Fig. 3 shows such a connection between the equatorial Africa and the north Indian subcontinent ranging overland, during the spring Equinoctial period (also marked by various ailments – allergens, virus and vectors). One part of the feeder extends into (toxic) Western Europe. The mixed-stream flow spans the entire tropo-equatorial and temperate belts meridionally and descends into the Indian peninsula. To minimize the effect of such (mixed) down-draft, the natives on the ground wear turbans as headgear, day long (supporting information). And Indo-African human-labour exchange has also come into motion since c.1850.



**Fig. 2.** Imaginary line A-to-B runs through the 5 plateaus. Line C-D is the shore line. ACD are points on the 16° N lat. Kp=Koraput Kandhamal; Sp=Similipal; Jp=Jharkhand; Slp=Sikkim-Shillong; Mp=Mizoram-Manipur plateaus. Vp = view point approx at 91°E/20°N. The 5 radians marks the lines of forcings of the sea-atmosphere couple

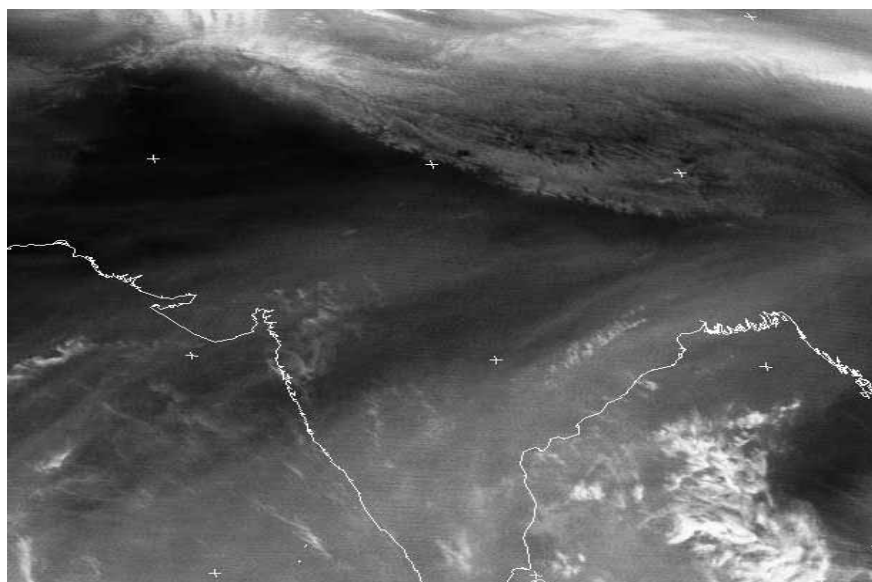


**Fig. 3.** Planetary scale, moisture in stream flow mode; spring Equinox 2012, 00-UTC; IR 5.7 – 7.1 μm, geostationary; curtsey – Dundee University satellite service

Drug resistant strains also differ within Asia. And, historically (since c.3<sup>rd</sup> B.C), there has been an extended connection between India-Sri Lanka - Malayadesa (Malaysia) and - Balidesa (Indonesia); Kambodha (Indo-China) i.e., the whole of Asia in human and animal exchange programs. Fig. 4 shows a similar atmospheric vectoring connection between Sino-



Indo China regions towards the Deccan –cum- the intense malaria prone eastern coastal regions of the Indian peninsula during the winter solstice i.e., regions of low outgoing long wave radiation (OLR). The swerve is due to Coriolis. This apart, the north Indian plains and the Himalayas are year round effluxed by atmospheric stream flows from central Europe (data not shown), due to gravity (exerted by Tibet-Himalaya geomorph). Thus, annually the whole of the Indian sub-continent's (meteorological) atmosphere experiences extra mural injections from 3 directions (is not unidirectional as is the case with most other nations). The day may not be far, when new strains will emerge having the worst of the Afro-Asian strains, as mixed features. Thus enlarged challenges are on the horizon. Malaria is here to stay and also act as a propeller of advanced research; man-hour engagement; with ever heightening public funding (Fig. 3 and 4, curtsey Dundee Sat. Centre, Dundee Uni. Ori. Source, eumetsat VISSR (IODC) 057.0E Quicklooks).



**Fig. 4. Planetary scale, moisture in stream flow mode; winter Solstice 2011, 00-UTC; IR 5.7 – 7.1  $\mu\text{m}$ ; geostationary; curtsey, Dundee Uni. satellite service**

It is well known, that physiologically, among all the age groups, the juvenile offers the best humoral condition. And, humoral support (anabolic) provides fillip for initial parasitemia from skin stage-to-hepatic stage. Due humoral involvement, heightened erythropoiesis sets in, because severe parasitosis, precipitously. Malaria + Chemotherapy (i.e., CQ\ACT\ Lumefantrine\Arterolane\Piperaquin) induce hemolysis cum erythrolysis; nephritis; myocarditis, etc, and acute inflammation. And, non-humoral support {catabolic/menopause stages}, which is also marked by an ever present inflammation {non cell mediated}, assists individual specific mutagenesis. Jointly, all this contributes significantly in confounding the dose regimen and confabulate with the known mechanics of the current group of modern anti-malarials (which are all chemotherapy compounds). Juveniles also mingle the most and additionally facilitate transmission. The Indian census indicates that among her sub-populations, the juveniles-adolescents form the largest group. Hence, large affliction number will stay put. Blocking transmission in such a domain would be the toughest test for any safe drug.

Thereafter, the geriatric and specially the status menopause groups (also enlarging census) offers the most conducive non-humoral support for the emergence of pernicious mutant strains, their survival, with low symptomatic and asymptomatic clinical status causing the evolution of obstinate resistance to drug. Subdued/absent hormone is the unstated principal cause of low parasitemia. The geriatric menopause group therefore, also acts as a large mobile stock pool and jointly cum severally retain transmission (of high virulence) in an ever active state. In drug discovery, the resistant juvenile and/or the geriatric groups, in core endemic zones are not focused upon, exclusively, least being the menopause group. Furthermore, in the endemic remote of the rural regions, concurrent poly protozoal infestations {protozoal/helminths}; tick borne infections\infestations {trypanosoma}; bacterial; viral; filarial; and even with tuberculosis are encountered. In all such cases, malaria is the dominant at clinical presentation. Post anti-malaria therapy, all such underlying/dormant infestations\ infections leap to the fore. This confounds diagnosis, often being treated as 'brain malaria' (complicated malaria). This also complicates prognosis and finally gets to be erroneously marked in the official records. We therefore opted to FMH. Overtime, the Koraput model matured to take in all these into its swath (not pre-meditated).

In this communication we report the prophylactic and the therapy effect among all such groups (using only OMARIA). We have relied on the simple field microscopes (gold standard) for real time simonic evidence out in the field/clinic, by the treating clinician, and specially by multi-disciplinary teams/individuals. On *datum* basis, the multi-lateral operation-MIM [19] and 'Fight Malaria at Home\Ghare Maro Malaria' cum 'OMARIA' (1998) were initiated on ground in near similar period, in two continents. Either follows the NMEP-1958 (see Ref.6), which had transpired out of the NMCP-1953 (see Ref.5). The commercial African Malaria Vaccine Testing Network - 1995 [20] was subsumed into the societal AMANET only in 2002 [21] and then came the Roll Back Malaria [22] with WHO partnership - 2002 [23]. Gradually up came the MMV [24]; the NRHM-2004 (see Ref.8); the White House Initiative-2006 [25]; 'UNICEF-2006 [26]; Bill Gates Foundation -2008 [27]; the Global Fund-GFATM-2010 [28]; and of late, the Ireland based University College, Dublin research initiative since July-2012 [29] which with a twist has adopted our motto-phrase as '*fight malaria @ home*' and another spanning Ethiopia-USA axis-IRC, 2011[30]. Important is that, across the continents, there may be many such mini/macro efforts (yielding sterling results), which all need to be brought to light as each may benefit (enrich) from the other's model. The Koraput Model and FMH are bottom up concepts; have the community at its heart; relevance for the administrations and industry (drug discovery); is flexible; replicable and current (verifiable and participatable). FMH exclusively uses OMARIA.

## 2. MATERIALS AND METHODS

There are 3 types of *Punica granatum* Linn. 1) Pomegranate (English), large, reddish brown, leathery on ripening, large pea loaded, sweetest (aril), native to temperate and semi temperate climates, known as *Bedana* in Sanskrit and in other Indian vernaculars; 2) Also Pomegranate, same size, yellows on ripening, native to deciduous and tropical climate, next to *Bedana* in taste, medium pea, is known as *Dalim* in Sanskrit and in other Indian vernaculars; 3) *Dalimba* (small), a vernacular phone, is also known as *Punica granatum* L. It is native to India (Fig. 5 and 6), has mini pea, eminently harsh, thick rind, dries to stone hardness, has only therapeutic value and usage. No commercial or food value. No. 1 and 2 have thin rinds and other limitations.



**Fig. 5. Live Ayurvedic Dalimba (*Punica granatum*). Max. diameter 2 inches**

OMARIA is made from the sun dried rind of the year round fruiting (above No.3 type), native Indian tropical medicinal fruit Dalimba (Fig. 5 and 6). Such Ayurvedic variety is a unique natural member among the punica family. It is apparently exclusively native to India and is yet to be reported from temperate regions. Post pluck (best at chloroplast stage) the fruit is cut, its aril is discarded, the rind is bone dried to stone hardness in shade or in Sun, Fig-6. It is then hand pounded and filled @500mg., into gelatin capsules of size No.'00'. Season and region specific, the rind contains 25-35% ellagic acid; 65-70% ellagitannins with K<sup>+</sup> as anomer ≈ 10%. There are no confounding moieties, nor are the constituent moieties confabulating. All the constituent moieties are synergistic. We have been talking about the synergy between these compounds and the conventional drugs in various forums [31,32], as run up to this communication. Drug yield (specially tannins are low) from the plants pedicured with inorganic fertilizers and/or water *ad-libitum*. Within Indo-subcontinent, fruit's cross-section, aril content, harshness, and rind's thickness differ. So too vary the balance between the ellagic acid and the tannin moieties in relation to agro-meteorological domains. All this do not effect anti-hemoprotozoa efficacy. Empty gelatin capsules for effort FMH, have been 'donated continuously' by M/s Sunil Synchem Ltd., Alwar, Rajasthan, India, since 2004-05.



**Fig. 6. Ayurvedic Punica, best drug yield size, post whole sun dried & post granulation appearance**



### 3. HISTORY OF USE

From within India, there are no reports of any other public-private efforts alike the Koraput Model; FMH and OMARIA, being comprised solely of the dalimba. In India, the Dalimba has more than a millennia old history of use (in Ayurveda) in numerous ways and compositions for convalescence, hematinic, anti-dysentery (amoebaesis) and anti-diarrhoeal i.e., anti-protozoals, antimicrobials, anti-helminthes, and also as anti-hemorrhagic and anti-coagulants, etc. Always only the dermis is used in powder form (we too selected this due ready availability and economy). In Ayurveda, pyrexia has been intimately associated with malaria and pyrexia forms an exhaustive chapter termed 'jvara nidana' (see Jivananda's commentary on Susruta's chapter on visamajwara (sever fever); and in Madhava Kar's jwara nidana (fever determination). Specially, Madhava defines malarial symptoms via the phones kampa (rigor); trutiyaka (tertian) and chaturthaka (quartan), among other sub-types of fevers. And, fever has also been indicated as fatal. The designated drug compositions are numerous; are poly herbal, holistic, and come under sub-chapters like jwara naska (fever destroyers). Few of these holistic poly herbal jwara naska compositions do have the dalimba as one of the constituent, albeit among the lesser members placed in the low of the v/v or w/w order of the mix. Hence, do not yield any indication regarding its sterling efficacy vis-à-vis hemoprotozoas. Least of all its efficacy is against all stages of the parasite including/excluding gametocytes. Importantly, the principal herbs (top penta) in the jwara naska compositions are all non-Dalimba. The Dalimba in all such compositions in all the ancient/classical Samhitas (compendiums) is used as part of the holistic concept which is the hall mark of classical Ayurvedic formulations. The Dalimba is also noted in the compositions for numerous pathologies, apparently positing it as a pedant member (buffer; mass enhancer; etc.). It offers no inspiration whatsoever to even the most enabled in the trade about its efficacy/potency against malaria parasites.

*Vis-à-vis* the use of dalimba, even suggestive applied terms viz., obstinate/recurrent/cyclic fever or pyrexia are also conspicuous by absence in traditional therapeutic literature of the Sino-Mongoloids [33,34] and the older Ayurveda [35,36]. There is also no report (of use of Dalimba to manage fever or anything akin to blood parasites) also from the Nipponese, Maori, South and Central American, Egyptian, Grecian, Latin, Negroid, Unani, Arabian, Bactrian, etc., ancient cum medieval schools of historical and cultural medicines. Moreover, in the herbariums of these lands our candidate dalimba is not noted.

Nevertheless, some modern scholars claim that the anti-parasitic effect of Dalimba is 'well known'. The scholars of Botany, Sanskrit linguists and the practitioners of Ayurveda and gastroenterology disagree. Confusion is noted between colonic protozoal parasites (which is alluded to in the classical texts) with the hemoprotozoa of the modern sciences (a fact not known even on the momentous datum of Sir Ronald Ross, c.1900). Our studies also indicate that the Ayurveda clearly prescribes the Dalimba in diarrhoea and anecdotally in dysentery. It is well known that diarrhoea can be induced by change of (i) place and altitude e.g., hill diarrhoea (ii) potable water (iii) food (iv) psychological stress (v) puberty onset, etc. Dysentery can be induced (among others) by medication, alcohol, narcotics and even by opium, onion, glutton, animal fat (adipose), etc. All such conditions are independent of parasitic aetiology. Yet the Dalimba is prescribed and proves useful. Dermal infections are also parasitic. Ayurveda has plethora of compositions and formulations for fungal infections; scabies and dermatitis. And, not have the dalimba as a constituent ingredient. Therefore, the Ayurveda does not suggest any anti-blood parasitic role even to the erudite mind.

Interestingly, all the other ancient and medieval schools of medicines were and remained non-invasive, well past the advent of the redoubtable European surgeon barber associations -c.14<sup>th</sup>-18<sup>th</sup> A.D. [37]. Whereas, the Ayurveda was the sole school that had robust collegiums of learned practitioners of invasive medicine (Susruta being the foremost – c. 6<sup>th</sup> A.D.). In 1907, the German anatomist, Rudolf Hoernale [38] had in 1907 made a translation of the Anatomy chapters of the Charak Samhita (c.4-5<sup>th</sup> A.D., Ref.35) as compiled by Jivananda which is termed by modern researchers as Atreya-Charak system of Indian medicine, intonated as *Aayoor-Veda*. Rudolf has indicated that the ancient Indians never went to Greece to learn/imbibe any health care related science. It is the Grecians who used to. Similarly, it is the Chinese who visited Bharat Varsha (alias year round maintainer -India) to learn, and carried back copies of various texts (Ayurveda included). Even, few Hindu scholars and nobles post conversion to Buddhism had migrated to China as leaders, preachers, teachers and translators [39]. Atreya was the noblest of the Ayurveda schools of the 1<sup>st</sup> millennia B.C., (debatable lower dt.), while the fountain is ascribed to Dhanwantari of the 4<sup>th</sup> millennia B.C (debatable lower dt.). Yet the primal texts are bereft of any evidence that can be cited/used in any manner to relate the Dalimba with fever or even with blood disorders and or with general malaise. In the Hindu *alias* Sanatan (continuum/hydaspes) system, the apex scholar-members are known only by illuminating metaphors. The classical text of the Ayurveda is encrypted with perfect diction (for brevity) and also is embellished with (illuminating) metaphors.

This apart, the Ayurveda has texts pertaining to principles of practices. The primal being (vi) Dhanwantari Nighantu (vii) Bhavaprakash Nighantu (viii) Shaligram Vaishya's Shaligram Nighantu. (ix) Jivananda's Samhita, etc., (Ref.30 & 31). These practice texts have the postfix viz., Nidana (determination/investigation), Chikitsa (treatment), Vava prakasa (symptoms), Nighantu (formulation\pharmacy), Jivananda (life-joy), Dhanwantari (Midas touch), Vaishya (medicine specialist), Vesaka (surgeon), etc. Even the term 'shaligram' denotes 'fine grain/grinder' (pastel expert). The entire gamuts also do not suggest even remotely any nexus between Dalimba and fatal fever/blood disorders/general malaise (that is malariasis as we know it at present). Nor is the Dalimba mentioned in the post 1950 printed-in-India official texts pertaining to the indo medicinal plants [40;41], and their Euro-American inspirations [42-44] or in the classical recessions and recensions (published in the footsteps of modern models of Occidental compendiums) viz., Acharya Priyabrata Sharma's 'Dravyaguna Vigyana' *alias* science of medicinal qualities (Chowkhamba, Benaras Hindu University). Even, the (Indian) National Research Centre for Pomegranate has not reported any anti-malarial use [45]. In brief, history of *punica* usage indicates that it has never been used for managing fever and/or malaria. Hence, vis-a-vis our caption, OMARIA is a new find.

In the west, information about the Indian scientific heritage started only with the erudite Englishman Monier-Williams (1819 – 99) and German Friedrich Maximilian Müller (1823 – 1900). But, neither had touched Ayurveda. More about the unknown, lesser known aspects and materials of Ayurveda can be had from Deepak Bhattacharya [46] and the book 'Indian Ancient Sciences' [47].

#### 4. COMPOSITION

*Dalimba dermis powder* 100% (100 mesh) taken either w/w @500mg/Cap., press-filled in '00' size gelatin capsule.

#### **4.1 Dose: Therapy**

1cap thrice daily at an approximate interval of 8hrs, for 3 consecutive days; (empty stomach -o.k).

#### **4.2 Location of Use**

Indian Red Cross Society (IRCS) ayurveda clinic, Koraput town, Odisha, India; 18°49'N/82°43'E.

#### **4.3 Dose: Prophylaxis**

1cap/500mg/day/head for the periods indicated.

##### **4.3.1 Location of use**

At village level; further away into the remote, by visits and stay put e.g., Narayanpatna, etc.

### **5. RESULTS**

#### **5.1 Therapy**

The IRCS clinic has been dispensing OMARIA since June-1998. Till date it has dispensed to >16,000 afflicted patients. The data being very large we discuss the Zeist in brief. Clinical microscopy indicates that, OMARIA therapy is potent *vis-à-vis* the gametocytes of the either sex. Falciparum predominates as determined by the double chromatin ring in the fixed slides. This apart, the parasitized erythrocytes rapture precipitously even on being exposed to sub-clinical doses of OMARIA-releasing the immature merozoites, thus terminating the malady precipitously. The circulating hemoprotozoa become less pathogenic within 2-4hours of the 1<sup>st</sup> dose {impotency of the parasite is felt}. Post the 2<sup>nd</sup> dose (16<sup>th</sup> hour) clearance mechanics sets in. There is a marginal rise of the parasites in peripheral blood slides ranging the next 12-24 hrs. Ostensibly, the parasites move towards the central circulation in order to avoid the ellagitannins – the large moieties of OMARIA. These moieties apart having longer life (than Ellagic) being hydroxyl-centered compounds have affinity for the musculature/periphery i.e., exert high tissue perfusion force. Thereafter (post the 6<sup>th</sup> dose; 48<sup>th</sup> hr), rapid clearance sets in, and the native is bereft of any parasites from around 36<sup>th</sup> hr. In-between, kill of the circulating mature gametocytes sets in pre to the 24<sup>th</sup> hr., from the 1<sup>st</sup> dose, and clearance of gametocytes occurs pre to the clearance of the non-gametic parasites. The Ellagic acid acts (more) rapidly and has a pronounced affinity for the hepatocytes. Our considered view is that, OMARIA blocks transmission and also is very effective against all stages of the malaria parasites.

#### **5.2 Transmission Block Aspect: Whole Village Resistant Geriatric Group**

A 'Whole Village Prevention Program' - was conceived and organized by the Secretary, (district) IRCS cum District emergency section along with the District Program officer, in association with the Red Cross medical officer (Ayurvedic). It was run under the overall superintendence of the District Collector cum District Magistrate. All the 3 villages are in Koraput district, well outside the district H.Q. The villages were identified (by the

Collectorate) and prophylaxis modality was run (by the Red Cross and Emergency and Program sections). The 1<sup>st</sup> dose was administered from 07/07/2003 to 13/07/2003, then intermission. The 2<sup>nd</sup> dose was administered from 07/08/03 to 13/08/03, then intermission. And the 3<sup>rd</sup> was administered between 07/09/03 to 13/09/03. Every resident was administered OMARIA. All the febrile members of the groups in all the villages got cured of malaria (therapeutic effect). And, these members remained recurrence free ranging between 6-36 months. Prophylaxis followed. Individual specific prophylactic response was noted – for the 1<sup>st</sup> time. We also noted that, the geriatric abhorred mosquito nets, and Sep., is entomology bloom period in the locale. We learnt later that the group also had few cases of sickle cell (were most vocal about the smooth efficacy of OMARIA).

Table 1 gives the summary of the result of OMARIA in the 3 villages as an oral prophylaxis candidate in the geriatric group monitored for 1 year period post cessation of the modality (intermittently thereafter. OMARIA service is still available in these villages as on date). Such prophylaxis was clinically observed wherein inoculation and transmission pathways were entirely open-in either sex. The inclusion of all the members provided to us an early expouser *vis-à-vis* the tertian geriatric group (i) OMARIA's efficacy (ii) the atypicalities associated with the pathophysiology of such group (iii) OMARIA vrs sickle cell. Clinically, all the members of the group were of tertian category; lived bare foot, frugally dressed; consumed liquor; did not use mosquito net, and were assumed to be either only *vivax* carrier and or mixed with *falciparum* (determination devices being not available). In other words, the *plasmodium vivax* (ostensibly) was possibly also getting killed and cleared by OMARIA.

**Table 1. Therapeutics cum prophylaxis results along with long period observations of drug-dose effect in drug resistant geriatric group, by adopting 3 whole villages**

Village	Total homes	Total inhabitant	Geriatric*	Malaria incidence
Badamput	35	173	10	Nil
Gunthaguda	26	119	6	Nil
Mundaguda	27	119	10	Nil
Total	88	401	26	-

\*Visual assessment.

The geriatric group broadly were of 2 types (a) asymptomatic gametocyte carriers that required brief medication of 500mg/day/adult for 3 consecutive days (b) obstinate tertian status (ultra resistant i.e., pali jwara candidates) having mono and mixed infestations that required a sustained 15-21 day period therapy @ 500mg/day/adult - sustained sub-clinical dosing. In all such cases, post the therapy period not had any gametocytes. We felt, OMARIA indeed blocks transmission, whereas, anti-gametocidal therapy is rare [48]. The drugs that are noted to be anti-gametocyte are also very toxic to the human physiology [49]. OMARIA is not. OMARIA is very potent against gametocytes, yet non inflammatory [50].

The geriatric group (less-focused) turned out to be the most obstinate carrier. They have (in villages non medicated with OMARIA) thus far defied all attempts of sterilization *via* chemotherapy made by governments and by the multi-lateral schemes. All this ignited focused interest towards the age-old resistant tertian cases (specially geriatric pali jwara members). Even in such challenge group, OMARIA's moieties indicated that it had a considerable in-blood life - evidenced subsequently by others in parts [51], with lymphocyte specific anti-inflammation effect. Inflamed lymphocytes return back to normal architecture. The geriatric is also in a constant state of inflammation (specially in the focus domain), subsequently determined microscopically. Even in such challenging conditions, OMARIA

suggested that it also had a potent anti-inflammatory cum anti-oxidative prowess (process scavenging) in-vivo, systemically, that is not the feature of any other anti-malarial. Subsequently evidenced by others in parts [52,53].

### 5.3 Transmission Blocking Aspect: Adolescent /Juvenile Group

All conventional anti-malarial drugs are chemotherapy. Which is why they induce side effects (in all age groups, and specially in geriatric/catabolic stages) and are most contradictory in anabolic stages. Adolescent is a unique anabolic stage in the development biology of the anthropomorphs (growth hormone active phase) marked by (i) heightened response to pathology (ii) variable therapeutic response (iii) non-uniform inflammatory response, being the hall marks. Paradoxically, the protease caspase-12 is pro-parasite and limits elimination [54]. Is inflammation intensity dependent; upregulator and humoral i.e., expression is high in the juveniles/adolescent (supporting information). The sarco/endoplasmic reticulum  $Ca^{2+}$  - ATP's ortholog of *falciparum* spp. (*pfatp6*) has been suggested as one of the potent targets for drug efficacy. However, polymorphisms of *pfatp6* gene before and after exposure to conventional drugs have been reported (even) from low transmission area, and more so in the humoral stages, and Koraput\Narayanpatna is ultra high transmission area. Drugs that work via the *pfatp6* ortholog indicate excessive swings in efficacy in the hormone active groups (clinicians abhorre swing). Iodine is advised as compulsory supplemental food additive at anabolic stages. Iodised salts also fail drugs that work via the *pfatp6* ortholog (ongoing observation). Iodine also upregulates parasitemia. These are additional cause of drug failure and/or in low efficacy than the label and/or idiopathic results. Few cases of sickle cell are a possibility in our sample (not determined). Therefore, sustained observation involving juveniles becomes necessary.

Narayanpatna is located in the lower niches of the Niyamagiri hills, Koraput, Odisha, India, 300-400mt., above MSL, which is an hill system of the ancient Gondwana (geological period). These hills in the traditional indo-literature; geological; geographical; meteorological; administratively are known as the 'Eastern Ghats' (precipice), and in history texts as *atavika* (high lands). The demography here comprises of (iv) *adivasi* – original inhabitants (v) mixed stock. Their nativity is alluded to in rock edicts dt. to c.3<sup>rd</sup> B.C. The lie of the terrain is towards the BoB in a south-east axis and presents an agro-meteorology of tropo-equatorial moist condition throughout the year with dense-lush green tropical foliage and numerous meandering perennial hill streams and brooks. Vector bionomics is a well known cause in the endemic character of malarial. Temporal character has also been indicated across the BoB [55]. The focus region is very conducive to vector bionomics. Being militancy prone the administration has its intent focus on such region and hence state sponsored free health service and products are available in good measure. The locus in a sense is difficult territory. It is also a priority administrative input block from the perspective of welfare programs. Hitherto, on 21-01-2010, was invited OMARIA to FMH in 4 tribal residential schools (RS). It was identified by the Block Development Officer (for OMARIA prophylaxis), and is run by the Block, Welfare Officer under the overall superintendence of the District Collector cum District Magistrate. Prophylaxis operations commenced from July. The RSs had an annual malaria episode score of 5-6 bouts/scholar i.e., the entire geographic domain had a year round incidence. 940 borders and 212 day scholars (total 1152) were apportioned to OMARIA by the Dist. administration to FMH with prophylactic regimen. Only the borders were adopted in 07/2010. Day scholars were left as challenge cum control. Table 2 gives the details (Last reviewed by multi-disciplinary team on 04-07-2012).



The 4 schools are located in various places within an local administrative area of 15Km<sup>2</sup> of Narayanpatna Block (OMARIA use is also additionally approved by the elected body known as *Panchayat Samity* ~ representatives committee). The day-scholars i.e., the non medicated group continued to have bouts of malaria, and were treated with CQ during every episode. Thus the day scholars in every school acted as 'control' cum 'live carrier mass' who freely intermingled with the 'OMARIA medicated mass'. Day scholars come-in from different villages located in various locations around the schools (walking distance). Their family members, neighbours and co-villagers were active carriers and resistant carriers, many of whom be gereatric, many were having acute defervescence cycles (active phase). Hence, transmission pathway - from the villages into the school - was entirely open. Additionally, the school compounds, the hostel tenements and the lush foilage had relevant healthy active vectors and often a day scholar would stay back in the common hostel (no quarantine facility). Thus, inoculation pathways were also left open entirely. Yet, transmission failed through the Indian monsoon (June-Sep), whence vectors prefer indoors diurnally and also nocturnally. Transmission also failed in the following warm-moist sunny periods (Oct-April) with cool nights, whence the blood meal preferring vectors (poikilotherms) go indoors nocturnally and to the out diurnally respectively, for seeking warmth/sun bathing -alongwith the homeotherms. And, the greater region is well known for entemological bloom. No inclement weather occurred during the period, therebefore or thereafter so as to have any adverse effect on vector biology, flight bionomics or populations. Fumigation was also never done. Thus, OMARIA presents the conditions of transmission blocking. All this is not experienced with any other anti-malarial (conventional\herbal) in the locale.

### **5.3.1 Dose**

In the 1<sup>st</sup> month, 1 capsule was consumed per head, every week i.e., 4 cap., in the 1<sup>st</sup> month. In 02/2010 no medication was given. After 1 month gap, only 1 cap per head was given in 03/10. In April, 2 doses were given (to cover summer vacation; boarders go home). In July and Sep., each boarder was given 2cap/head/month {total 11cap/head~9months}. No other drug or medicated food were taken i.e., non confounding status was ensured. Table 2 also indicates that only 10190 caps., (5095gms) was consumed by 940 candidates = 5.4gms of fruit rind powder intake by each candidate, spread over 276 days (wt. of the empty gelatin, not accounted). The average body weight being 30Kgs, it works out to only 652µg/kg of crude powder/day. As per the various *in-vitro* works, the crass yield of ellagic acid moiety is 3.25% and the ellagitannin duo is 6.75% of the crude whole powder, respectively. This works out to an order of 21.19 µg/kg and 44.01µg/kg, respectively, which =  $1 \times 10^9$ : 652. In other words, the ratio between the drug moiety and the body mass is of the order  $\cong 1$  unit of drug moiety: 1533742.33 units of body mass w/w (attain asymptomatic status threshold). This suggests, *in-vivo*, OMARIA is potent *vis-à-vis* the *plasmodium*. The entire regions outside the boundaries of these residential schools continue to have year round incidence (almost every native is afflicted). The anthro bio-mass of the schools stand out as islands amidst a domain wherein year round manifests drug resistant cases. Effort OMARIA, continues. During the multi-disciplinary team's visit (4-7-12) it was again noted that the schools that are not under OMARIA – Fight Malaria at Home, scheme (in the neighbourhood) was having a current malaria incidence rate @ 5-7 afflictions/100 students (boarders\day scholars included).

**Table 2. Block, Narayanpatna; District~ Koraput; Province~ Orissa; Nation~ India. Ongoing OMARIA prophylaxis centre, 18°-50'47"N\83°-10'09"E**

<b>Residential school*</b>	<b>Period</b>	<b>Total day scholars # (boys and girls)</b>	<b>Total boarders (boys and girls)</b>	<b>Total no. of OMARIA caps., received and consumed</b>	<b>Total no., of OMARIA caps., consumed per head</b>	<b>Average no., of times Mir., affliction pre-OMARIA</b>	<b>Average no., of times Mir., affliction post-OMARIA</b>
Dandabadi	9 months	33	370	3080	08	05	Nil
Palaput	Do	48	190	2370	12	04	Nil
Kumbhari	Do	51	190	2370	12	06	Nil
Podapodar	Do	80	190	2370	12	07	Nil
4 Res. Schools	Do	212	940	10190	Avg. = 11	Avg. = 5.5	00

*# Day scholars, teachers and staff were not included. They were included in 2012.*

## 6. ASSORTED ASPECTS

### 6.1 Concurrent Infections and Infestations

Malaria is well known to be associated with the enlargement of the thyroid gland (thyroiditis) and tachardia [56]. The Medical Council of India, is of the opinion that CQ + Erythromycin (drug of choice against *typhosa*) cause cardiac failure [57]. Further, a dim view is taken of the practice to randomly prescribe CQ/ACT therapy sans microscopic confirmation (gold standard), specially when the administration has put in place multi layers of field mechanisms during the last half century. Against such background, concurrent infections involving typhosa and malaria are numerous in the focus geographic domain. In such cases, malarial symptoms predominate at clinical presentation (excepting tuberculosis). Typhoid related symptoms such as a thick layer of buff white/gray/yellowish matter on the afflicted's tongue with – non cyclic- deep seated obstinate headache, with near absence of sweat cycle i.e., subdued defervescence cycle and limited self ambulation ability (is not lost as is the case with sole Typhoid) are discernable only to an experienced clinician. Such types do not respond well to only antibiotics or to only chemotherapy (anti-malarials). Such types also do not gravitate to cerebral malaria status (are entirely miss-diagnosed; recorded and treated). In such cases, on application of only OMARIA/CQ/ACT (sans any antibiotic), malarial infestation clears, and typhoid leaps to the fore, which then gets to be misinterpreted as brain malaria; recorded and treated likewise. Thus, the Figs. in the Govt's., record, go up. All through (well post recovery) the WBCs remain inflamed/enlarged, which is viewable via the microscope. The afflicted tends to loose ambulation, necessitating swift SOS. If OMARIA be at least one of the candidates (administered as the dominant part of a multi-drug combined therapy as an all out combat effort to save a sinking life) the recovery schedule and the post recovery acute side effects, lingering myalgia, and long term fatigue, hypoxia, and anemia, gastritis, are demonstratively of short duration or nil. The native rejoins duty early.

Since the natives live off the soil, bare foot, amidst foliage, domesticated ruminants, pets, use no disinfectants, eat with fingers, concurrent infections and infestation viz., malaria\gut infestations by helminthes + filaria + trypanosoma + tuberculosis + viral + fungal + infected wounds + allergic sinusitis (any combination), are also encountered (few types being common). Across such spectrum, OMARIA is noted to be synergic cum adjuvant when administered along with the specific pharmacy (as part of MDT; allotropic or not). OMARIA also down-turns gastric reflux and other side effects, post oral ingestion of drugs.

Malariasis is a well known response pathology, which in turn is also individual specific. And, inflammation is the response. Microscopically, alterations in the cross section of the lymphocytes are viewable, also in all types of infections/infestations. If OMARIA be not one of the drugs of the MDT, the architecture of the inflamed lymphocytes remain altered, even post 'kill and clearance' of the malaria parasite. With OMARIA the inflamed lymphocytes regain architecture precipitously between 72-96hrs. This points in the direction (evidence) that the other drugs of the MDT induce inflammation on their own, whereas OMARIA does not (assists down-regulation).

In malariasis, mild alterations in the lymphocyte's architecture\cross sections, and in their total count set in immediately post the skin stage of the sporozoites which becomes normal during the hepatic phase. Architecture alteration is prominent during erythrocyte invasion and infestation stages. It is more prominent at vascular extravasation stage (cerebral malaria stage). In malariasis, host mediated inflammation is more due to an erythrocytic crisis

deemed by the physiology limited to the blood phase of the various developmental stages of the hemoprotozoa. The gametocytes do not elicit any such response pathology. Furthermore, while the plasmodium necrotises the hepatocytes [58], OMARIA posits as liver friendly (function improves); hematinic; apart from being potent anti-plasmosydal.

In the hills and the plateaus, tick borne disease cum malaria is also another feature. The ticks come mostly from the deciduous flora (some say ticks also come from animals !), and seem to be quite a few in variety (naked eye assessment). At presentation, pyrexia is high; slumping head (yet neck muscles not as slack as in cerebral malaria); sleepy; moderate palor; hearing loss; head reeling; myalgia; appetite loss; less/no sweat; anemia; erythrolysis; restless. The symptoms are somewhat alike Trypanosomiasis. Then, there are cases of malaria cum filaria, which present mixed symptoms (subdued). All such cases are obstinate in recurrence; the inter-episode periods are non uniform and as well be the paroxym period of each episode. The malaria + tick infection and the malaria + filarial cases are normally considered\announced and also recorded as that of brain malaria and as Pv respectively. In all such cases (i) OMARIA (1000mg) + (ii) dimethyle carbazyme is very useful (BD x 3 days). An adjuvant of 200-300mg of paracetamol ushers rapid relief, with the 1<sup>st</sup> dose. Any failure in diagnosis and in non application of the appropriate pharmacology (dimethyle carbazyme) prognosis gets to be grave or skewed (complication). It then too gets recorded as 'brain malaria'. It is now reported that a vector can inoculate either i.e., malaria and filarial parasites during the process of blood meals [59,60]. Thus are widening the vector spectrum\transmission pathways. Cases having infestation of malaria and filarial (blood and lymph involvement) are rare, and come in with general edematous limbs (even facial); deep fatigue; severe myalgia; low and near continuous fever; acute arthritic symptoms (as in Juvenile Rheumatoid Arthritis); strong appetite; clear tongue; and suggestive high BMR. Initially they are treated as cirrhotic lever and/or nephritis (reality being different). In such cases, OMARIA clears malariasis and limitedly down-turns filariasis. Whence OMARIA is administered with Dimethyle carbazyme, the native bounces back abruptly even with sub-clinical \ 2<sup>nd</sup> dose (supporting information). There are few malaria + tuberculosis cases (tribal people abhor TB and have own effective-radical treatments). At presentation, it is COPD that is dominant. Malarial symptoms are secondary, because of extra-large production of CO<sub>2</sub>. And, anti-TB medication is poorly tolerated by the natives. It gets to be better tolerated if co-administered with OMARIA bolus (buffer activity). Dengu is uncommon in the hills/plateaus while it is reported from the adjoining plains. In rare cases of Malaria + Dengu, - it is dengu's symptoms that predominates at presentation. In other words, in cases of virus + hemoprotozoa, it is the viral malady that confounds the symptoms at presentation. Thus OMARIA with its collinear wide spectrum anti-viral proves useful.

OMARIA's numerous mode wide spectrum property makes it an all purpose safe use limited adjuvant. Its smooth efficacy is valued much by the natives. Hence the scheme to 'FMH \Ghare Maro Malaria', was well received by the natives in the remote locations of the rural and also got propagated via the vernacular [61] and fillip via the national organs [62], by and by.

## 7. THE MENOPAUSE GERIATRIC

The pan-global primary objective is 'transmission blocking' (thus far been elusive). Therefore, the issue before the India administrations is 'transmission blocking'. The crux issue is, does an observation of a single *plasmodium*\*vivax* parasite and or a gametocyte, in the blood smear (gold standard) from a afebrile cum asymptomatic {non-medicated} native of an drug resistant endemic region, be very significant ? Our 2-decade long on-foot

experience based considered view is, 'yes indeed'. Such - carriers have more parasites in the central circulation (unless otherwise proven). Is the most potent carrier (also unmarked; least febrile; least complaining) and also the cause for re-emergence (via delayed action). A mono parasite can re-start a whole new cycle. Specially from the geriatric to the non geriatric. And, between the aged old male and the female, the menopause geriatric (due to altered humoral conditions) are the contributor of the most virulent (pathogenic), most drug resistant and most successful transmission(s) to the males, of all ages, specially to the juveniles and to those having healthy livers. And, OMARIA blocks transmission and is super safe.

In India, joint family system is in vogue. Among the tribal, and the non-tribal families, the grannies are the centers of attraction/connoisseur in homes, inclusive of even the very large joint families. Family re-union happens on and often (entrenched culture), and that be the mailing periods. In other words, the indo-ethnic family structure, systems, values, traditions and the overall culture, assists transmission. Malaria is here to stay. Hence lays the relevance of 'F M H' (*Ghare Maro Malaria*) with OMARIA.

## 8. DISCUSSION

Our geographic domain has numerous primary health centers (PHC), apart district Head Quarter hospital. Our general experience has been that, throughout the region, any fever is 1<sup>st</sup> announced as malaria and anti-malarial treatment is given forthwith. That is being true also in the 3 villages and in the 4 RSs pre to being ear-marked to FMH with OMARIA (Koraput Model). In the RSs post summer vacation, few boarders return with fever. They are instantaneously labeled as 'cases of malaria', sans any confirmatory checks (infrastructure is not possible). This has prompted us to arm the borders with an extra dose of prophylaxis on the date of commencement of annual vacation (from 04/2012). It has yielded favourable results. The cause factor(s) for such unambiguous transmission block for significant periods invites multi-lateral initiatives (land and lab). By the time of going to press FMH has been put in hiatus in these 4 RSs to observe (i) re-emergence (ii) withdrawal effects, if any.

In animal Frevert et al. [63] and in anthropomorph Prudêncio et al. [64] models, the sporozoites have been shown to necrotise hepatocytes during the sporozoite to merozoite developmental phase (in hepatic vacuoles). On one hand the fibrotic hepatocytes provides better conditions for parasite's initial evolution, survival and mutagenesis; on the other hand the occluded sinusoidal cell layer, and the adversely affected Kupffer cells of the liver (chronic malaria) thwart. Chronic malaria also adversely effects the liver apart from addiction to methyl alcohol and hepatitis (induced/viral). All this limits the sporozoite's ability for incursion, evolution and proliferation. This is because (in fibrotic liver) the apicomplexan (which has a high metabolic rate) suffers nutrient, ion and O<sub>2</sub> starvation. Hence the tribal native (specially the geriatric of either sex) prefer alcoholic drinks (even have own home brews). On full moon nights (are also vector active nights), tribal communities indulge in binge drinking-singing-and-dancing. Binge drinking is marked by asymptomatic status long post regain of normalcy (common among tribal adults). In nature, alcohol posits as a mild herbicide/weedicide. The plasmodium is an apicoplasm and OMARIA is also a mild herbicide (hence, also mildly mycotic; bactriostatic). In the malaria infested hill-plateau domains, alcoholism among the natives is a natural selection. It too is not going away.

The Koraput model being an altruistic public-private partnership has been frank and flexible from the beginning. It therefore, has been able to factor in the numerous field atypicalities as



they became apparent (in other words, nothing happened overnight). From neat public administration perspective, the Koraput Model has been able to deliver on the ground. From drug discovery perspective such approach is called as 'bottom up model' (e.g., the poly moiety combination of ellagitannin(s) + elagic acid + dihydroarteimisinin will be wonderful; semi/wholly synthetic). The model also denotes fruit based herbalism (alias OMARIA). Is economically sustainable for it is different from whole herb use based methods (destructive herbalism). It also seeks to maintain the ecological balance. In other words, the model permits the flora to flourish, gainful rural employment generation, the vector and the parasite to live and yet fail the dreaded malady at the anthropomorphic stages, economically safely and efficiently. Due such well perceived innate advantages the administration has by now extended OMARIA modality to around 15 residential schools (deep remote) having >1500 inmates spread over 5 administrative blocks. All are welcome to join such opportunity to 'FMH' i.e., *Ghare Maro Malaria*.

In the initial years (2000) of OMARIA modality we had determined biochemically and radiographically, that a healthy liver up-regulates malarial complication; with high parasitemia; poly organ involvement; fulmination (complications); gravitate towards cerebral status and also assists rapid onward transmission. Subsequently, Chotivanich, et al. [65] have reported that high blood glycerols down turn efficacy of certain anti-malarial drugs. Hormone replacement therapy; anti-hypo thyroid therapy and anti-hypertension therapy also downturn efficacy of the conventional anti-malarials. Not so much do they to OMARIA. Furthermore, neutral lipids have now also been indicated to be associated with haemozoin mediate efficient and rapid  $\beta$ -haematin formation [66]. Hemozoin has been held as the root cause of systemic spiraling inflammation and complication in malaria [67]. *In-Vitro* OMARIA is said to terminate such cascade in a dose dependent manner [68] is non toxic with least clinical swing and effective in Africa [69]. Resistant malaria in core endemic zone is also 'complicated' (pathologically individual specific). The most relevant aspect of OMARIA-of Koraput Model is that it seems to effectively block transmission be it resistant, complicated or not (also safe and smooth).

## 9. CONCLUSION

For well known reasons, it will be best for any new candidate therapy (like OMARIA) to pass a long period mono-station field validation and be of low potency. In trying and exacting field conditions, OMARIA seems to be achieving this. The notable points being: a) OMARIA blocks transmission; b) geriatrics of either sex act as stock pool of the most resistant strains and retain transmission in an ever active state; c) menopause oldies serve as the mutant stock pool and as fail-proof donors/ virulent transmission contributors; d) anabolic stages are most conducive for inoculation and up-regulation; f) juveniles are the most mobile transmission platforms; g) mature age uptake inoculation as well; h) alcoholic/fibritic\impaired liver down-regulates malarial, while healthy liver up-regulates; i) alcohol down regulates; and j) cases of high serum glycerol develop complications rapidly and also require bolus doses of OMARIA; k) in concurrent infections cum infestations malaria is dominant at presentation; l) mixed therapy (anti-bacterial\anti-viral + chemotherapy + paracetamol + Omaria) yields sterling results and *prima-facie* appears to be the way forward; m) in all groups, OMARIA exhibits non-relapsing (no recurrence) with efficacy of high order, is prophylactic and therapeutic in cases where all other conventional drugs fail and/or elicit acute side effects, and has synergistic effect vis-à-vis therapeutics and buffering effect on the side effects and on the contradictory effects of all other pharmacy of the allopathic MDTs; n) OMARIA can also concurrently prevent viral infections (see Ref.6;7) and is also apparently useful in tick borne diseases too, but unable to prevent or cure bacterial, fungal,

tubercular, lymphatic filarial infections) OMARIA seems to work on all the stages of the apicomplexan-*falciparum*, with no resistance observed. Moreover, the eastern shore board of India with its unique geography of plateau-plain geomorphology cum warm sea orography with monsoon agro-meteorology is a natural home for year round vector-parasite cycle survival and manifestation. Malaria is here to stay; and p) all such aspects necessitated the unique Koraput model (Fight Malaria at Home). Furthermore, the Koraput model posits as a profitable vehicle for the administrations to combat malaria. Herb *Punica* (indo variety) be also considered for protection and wider domain plantation. Since vaccine is yet some time away [70-72], worldwide, Koraput model types may be searched for and patronized to work towards an effective-safe-economic-therapy.

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## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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