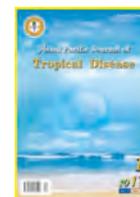




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Fight malaria at home: Therapeutic and prophylaxis clinical data

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ABSTRACT

Objective: To identify a new, safe and effective source to combat and prevent drug resistant malaria therapeutically and to make it as a home-made bio-medicine which is called as OMARIA (Orissa malaria research indigenous attempt) and use it on long term basis (decade) in mono clinical station and in field. **Methods:** The rind of a lesser known Indian indigenous fruit dalimba/ *Punica granatum* (*P. granatum*) is taken. Manual process to make a hand-made or home-made bio-medicine is done. Hand-filled into gelatin capsules and administered as an internal medicine. Therapy to 532 clinical cases is given at the Govt Red Cross Clinic, and Prophylaxis at site is administered to 401 cases by adopting 3 villages. **Results:** Hydrophylic, ellagitannins *viz.*, punicalagin (C₄₈H₂₈O₃₀; mw 1100~1125), punicalin (C₃₄H₂₂O₂₂; mw 780~785), ellagic acid (C₁₄H₈O₈; mw 302) and K⁺ co-exists as the only drug moieties. OMARIA has no other confounding or confabulating compounds. There is non alkaloid. **Conclusions:** OMARIA delivers therapeutics and prophylaxis to drug resistant *Plasmodium falciparum* (*P. falciparum*) cases. There are no side effects and no contradictions. Non-toxic at bolus/loading doses. No case progressed to cerebral malaria. OMARIA is a first time work. Original report on pan global basis.

1. Introduction

Orissa is a province on the eastern sea border of India with 30 districts, whose residents are vulnerable to the year round incidence of malarialiasis. In the focus zone, many families including infants and the infirm get afflicted by malarialiasis for 1 to 6 times a year. Although, on all occasions, a full regimen allopathic (conventional) curative chemotherapy is prescribed and availed for free at government owned and managed primary health centers and hospitals.

Despite the fact that India has a wide network of rural health service, a vibrant indigenous school of medicine, and strong multi-level inter-governmental and intra-governmental initiatives in combating malaria have also been taken during the last 50 years, *Plasmodium falciparum* (*P. falciparum*) continues to strike with undiminished intensity.

In Figure 1, the geographic location of Orissa/Odisha is marked by an arrow. Koraput district (KD) and OMARIA centre (OC) are also indicated. The district has a geospatial area of 800 km² with a census of 1 million. It is among India's core endemic zone of drug resistant *P. falciparum*

which has a year-round high incidence of systemic malaria and fatal cases of cerebral malaria[1]. It is also 400 km away (remote, rural setting) from the provincial administrative capital. The ethnic sub-populations are mostly tribal and all have very low levels of income. Hunting and gathering is still a way of life. All the inhabitants have similar living and working standards. They sleep on floor in mud houses without mosquito net. Humid condition prevails for half of the year. Apart from conventional / allopathic drugs such as SOS, they prefer alternative medicines. Hence, non-uniform genetic cum acquired resistance, variable response to known contradictions of the chemotherapy group of anti-malarial drugs (which per say they do not prefer) are offered. The region has a large number of mixed-poly carriers *i.e.* *P. falciparum* and *Pv*, *P. falciparum* and Bacterial, *Pv* and Bacterial, *P. falciparum/Pv* and cytomegalovirus. This decadal drug-dose use response is the first focused report from this remote drug resistant malaria core endemic location. Particularly, vector control programs having failed and also having contributed to the toxification of the habitat, at home makable economic remedy therefore had become very necessary. It was thought that it would be ideal if the family, as a unit, is able to overcome malaria at home. We report the use of OMARIA (Orissa aalaria research indigenous attempt) which is a hand makable herbal capsule (bio-medicine) with a wide spectrum efficacy and holistic effect.

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It is made from the rind of the year round fruiting Indian native medicinal fruit dalimba. This medicinal plant can also be grown all over the tropo-eqatorial climate-Latin America and mediterranean regions. It yields ellagitannins which are organic acid moieties *i.e.*, non alkaloids. From our use based experience and corroborative study, ellagitannins posits as more compatible physiologically than alkaloids as anti-malarial.



Figure 1. The geographic location of Orissa.

The use of OMARIA started in June 1996 as a mini food based economic remedy for rural homes and went on to find large scale of clinical application from June 1998 by the Indian Red Cross Society Ayurveda Dispensary, Koraput, Orissa, India, under the aegis of District Magistrate cum Collectorate[2]. In relation to Dhingra N *et al*[1], we find that the data are not in consonance with the reality of Koraput district.

Popular aspects of OMARIA public use was also collinearly put in public domain on a year to year basis as one part of community at heart policy[3,4]. It came to be known as Fight Malaria at Home[5]. It is not donor driven. This paper sets the invention component. It is the first decadal collated presentation of data pertaining to clinical and field use of OMARIA.

Punica granatum (*P. granatum*) is a fruit known as "dalimba" in Sanskrit. There are three types of *Punica*: 1) Pomegranate, on ripening becomes leathery reddish brown, grows normally in the temperate and semi temperate climates. It is known as bedana in Sanskrit and in many other vernacular; 2) dalimba, commercial grade, is a lesser species of Pomegranate. It is the same size with pomegranate, yellows on ripening and cultivated seasonally in deciduous conditions; 3) dalimba (small) which is native to India is usually grown in kitchen gardens, year round fruiting. It has only therapeutics and no commercial fruit or food value. It is less than 3.5 cm in diameter (Figure 2) and considered as a wild variety. As a bio-medicine, it is described for its medicinal use in the Ayurveda and in all classical texts of the ancient Indian school of plural medicine[6,7], which in turn has an umbilical connection extending to Vedic periods ~ Atharva Veda in particular. In India, the first and second species of *P. granatum* that referred in preceding part of the text are not used in Ayurveda

formulations while the third has more than a millennia old history of use in numerous ways and formulations other than for fever. Its use is mostly indicated for convalescence, hematinic and anti-diarrhoeal. In other words, Ayurveda as in various recessions and recensions of Charakh[8] does not use dalimba in malarial or to manage pyrexia. Whereas, pyrexia is intimately associated with malaria in any type or intensity.

Use of dalimba (Figure 2) as an anti-malarial along with the use of suggestive applied terms (*viz.* fever) is also conspicuous by absence in traditional therapeutic literature of the Sino-Mongoloids, Nipponese, Maori, South and Central American, Egyptian, Grecian, Latin, Negroid, Unani, Arabian, Bactrian, Homeopathy, *etc.*, ancient cum medieval schools of non-invasive medicine including Ayurveda[9]. Thus arises the invention component.



Figure 2. Indian native *P. granatum* – dalimba.

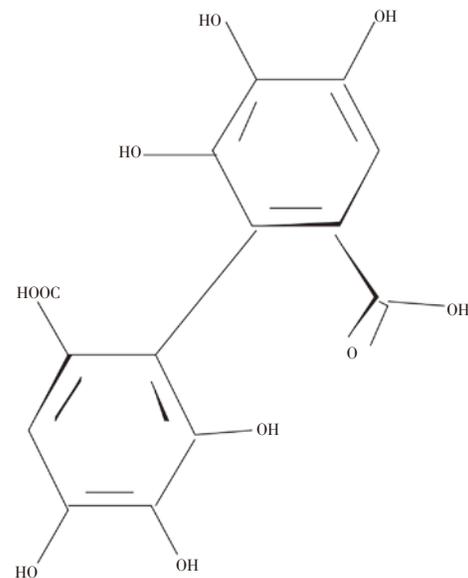


Figure 3. Chemical formula of ellagic acid.

The rind of dalimba contains ellagic acid ($C_{14}H_6O_8$; mw 305 as in chestnut bark, Figure 3), ellagitannins *viz.* punicalgin, punicalin and punicafolin, which are all tannin moieties and are derived by hydrolysis in the gastric chamber along with K^+ (own data). Figure 4 and 5 are the structures of the specific ellagitannins ($C_{48}H_{28}O_{30}$ and $C_{34}H_{22}O_{22}$) having mw

1100~1125 and 780~785 respectively. We know that large group of hydroxyl are well known as processing scavengers (anti-oxidative). Following our clinical works, Sreeram *et al*^[10] reported that Bedana – the commercial grade of the pomegranate species– also have ellagitannins along with K^+ , which is also known to have low yield and has confounding compounds, and shorter shelf life.

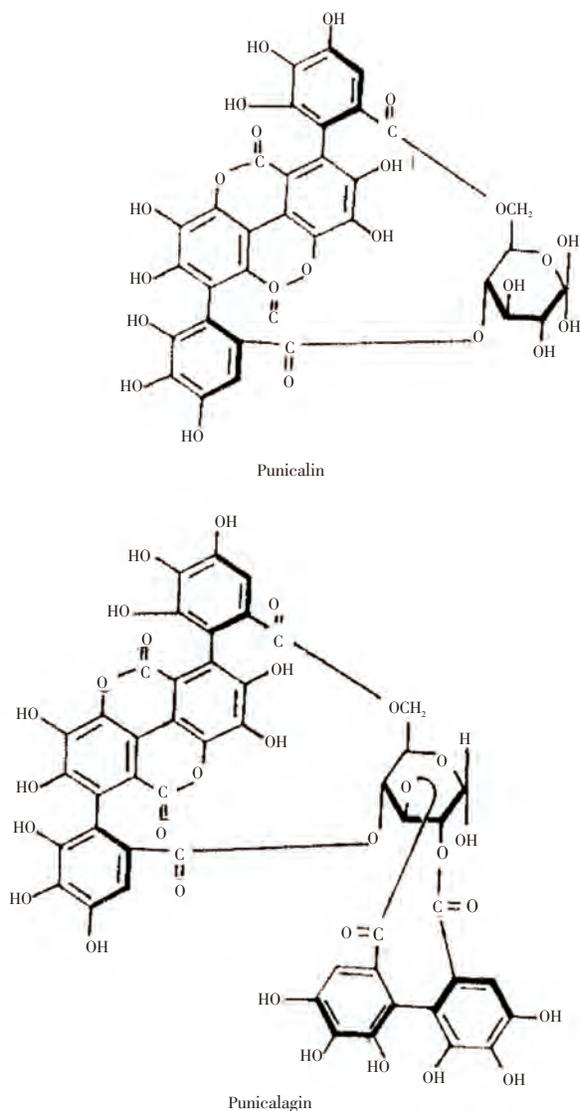


Figure 4. Chemical formula of punicalin and punicalgin.

It was followed by Mario *et al* who reported insignificant anti-plasmodial activity *in vitro* for non-*Punica* (other phyto) sourced ellagic acid^[11]. However, such findings have been contradicted by the work of PN Soh *et al*, who have also used non-*Punica* sources (ellagic acid)^[12]. This suggests a species and agrometeorology based variation and/or due to extraction processes, media, *etc.* The Indian native dalimba's rind (Type-3) has a consistent yield, and consistent volume or weight based efficacy. There are no confounding compounds and has excellent shelf life under torrid, tropical humid, open room conditions, which is the reason why we have also chosen it. Importantly, pre to our use (1998) there was no reported use of the moieties as in Figure 3 to 5, for treating malaria.

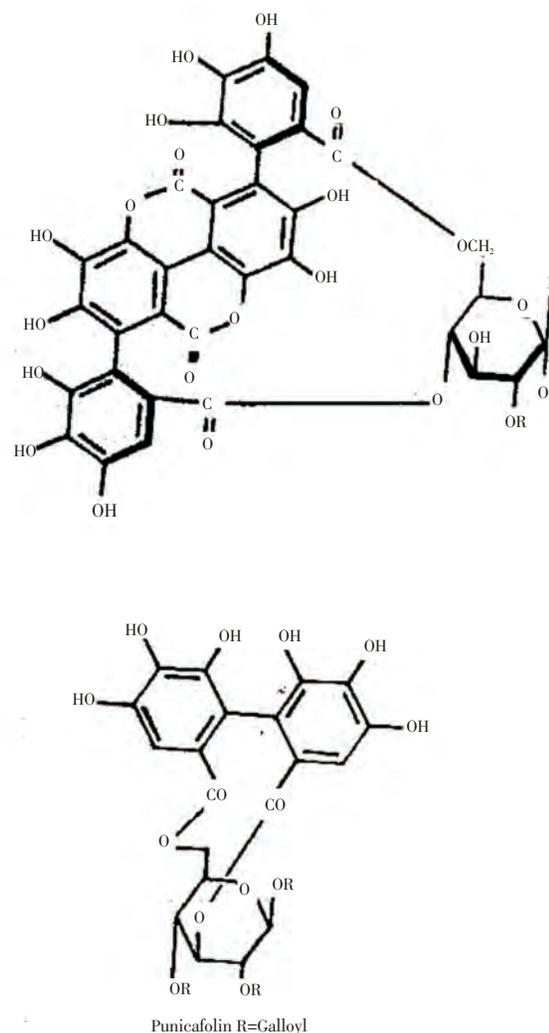


Figure 5. Punicafolin

Following our continuous, open and frank use of OMARIA in large scale of fields and public awareness of campaigns, Reddy *et al*^[13] reported anti-plasmodial activity in bedana juice (*Punica* Type-1) while L Verotta *et al*^[14], reported anti-plasmodial activity in other species *in vitro*. C Nepka *et al*^[15] reported tannins having down-regulate xenobiotic effect and being anti neoplasia and anti-cancer. Verotta's, Nepka's and Soh's group works (along with all others) provided additional basis and fillip to operations of Fight Malaria at Home. Yet our work by ourselves remained due for report.

NaCl deficiency leads to hyponatraemia^[16]. Remote rural regions such as KD and OC do not have supplies of physiological saline or the trained manpower for intravenous infusion. However, there are supplies of crude and state sponsored iodised and non-iodised common salt. Iodised salt has been reported as calorogenic which triggers polyphasic interaction^[17]. Our study also indicates that iodine assist heightened parasitemia, because malarial pathophysiology is also a case of ever heightening defense response against host's own red blood cell (RBC) with commensurate erythropoiesis (separate communication). Therefore, we have devised an easy village level technique to de-iodise NaCl.

2. Materials and methods

2.1. OMARIA making

The dalimba is plucked at chloroplast stage. Fruit is cut. Aril is discarded. The rind is bone dried in sun till stone hardness. It is then manually pounded to fine powder and is hand filled into gelatin capsules of size No. '00' at 700 mg per capsule (Figure 7).

Empty gelatine capsules were most kindly provided for free by m/s Sunil Health Care Ltd., New Delhi.

2.2. Process of the crude/iodised NaCl

Crude or iodised NaCl as available in the rural household is put in an earthen pot with 1/3 space empty while the mouth is covered with a clay lid and then sealed with wet clay, the pot is then burnt in charcoal hearth until red hot (600 °C–700 °C). After the air is cooled, clay sealings are removed and salt is gathered and ground to a fine mesh.

2.3. Therapeutics dose

The OMARIA was administered 3 doses/day comprising of 1 capsule (every 8 hour/day) for 3 to 4 consecutive days comprised of a total of 9 to 12 doses; case specific as clinically was assessed (gross 6 – 8.5 g of herbal powder only over the 3–4 day therapy period). All persons above age 8 years old were to swallow with potable water as vehicle. Children were to mix the capsule content (powder) in water and drink the supernatant after 2 hours of efflux. Amorphous, iodine free NaCl (20% w/w) is provided along side as optional to clinically assessed needy cases as supplement because rural cases often report at very late stage post infestation and were noted to also suffer from hypovolemia. Also, to preempt hyponatremia.

2.4. Prophylaxis dose

In July 2003, the Secretary, District Red Cross Society, officer-in-charge of the District Emergency Section and the District Program officer under the superintendence of the Collector-cum-District Magistrate introduced OMARIA in three villages as a Whole Village Comprehensive Prevention Program. Drug dispensation and all clinical matters as usual was to be done by the Red Cross. In 2004, a fourth village was added. The data pertaining to the fourth village (Panaspur) is not show for it also incorporates an advancement, which is reserved for subsequent report. These villages are apart, in January, 2010 the administration established its grass root level elected institution (Panchayat = democratically-people elected local body) and apportioned OMARIA to 4 tribal residential schools with 1138 students. Day scholars have been excluded. The remaining 937 boarders are all involved. Only boarders were given OMARIA to observe the contrast picture and transmission blocking aspect. These schools are located in the midst of thick tropical-humid flora and a region having very poor communication. Prophylaxis was initiated in July 10th, and 4 monthly doses have been completed. For the first month the students was given 4

capsules in 4 weeks, after 1 month gap only 1 capsule was administered per month in September, November (2010), March and April (2011). Summer vacation commences from May Day. Hence children were altruistically given 1 additional dose because when they returned to their homes, they would face more challenging inoculation conditions. The school authorities have already reported a drastic fall in malaria incidence among the borders.

Prophylactic dose for the other 3 villages had comprised of 1 cap/day for 2 consecutive days/week for 2 consecutive months (reduced subsequently during the year). For children below 8 years of age, contents of 1/2 or 1 capsule was dusted, mixed with honey, licked or swallowed twice daily. All above the age of 8 were to swallow with potable water as vehicle. Pregnant are not included. All others including lactating mother and child were to be given using ensured compliance and every aspect was monitored on weekly basis.

3. Results

3.1. Therapeutics

Blood slides down during pendency of OMARIA regime indicating complete parasite clearance within 72 h. Repeat slide films after 72 h, and again between the 7th and the 10th day and in subsequent months (in select known resistant cases) indicate nil deviation of the blood picture from normal. Nil relapse nor any silent mutagenesis was observed. Once clinically cleared completely, most of the cases thwart reinfestation ranging between 6 months to 4 years (why and how subsequent communication). Such therapeutics was reported and clinically continues to be observed even when the native works, lives, stays mostly bare-bodied in mud houses amidst moist tropical evergreen flora and sleeps without mosquito net in core drug resistant *P. falciparum* endemic zone or even when they commuted or immigrated for short periods to non OMARIA medicated drug resistant endemic regions or co-habited (net-less) with affliction active drug resistant historical carriers in common tenement having effective carriers. This meant blocked transmission, in spite of inoculation.

Table 1 presents the results of the cases treated with OMARIA up till 2004. Pregnant mothers was left out and taken later on. The table does not indicate any drug taken by such candidates. Later on they took for OMARIA as data from various corroborative experiments and clinical observations indicated that OMARIA is physiologically compatible. The clinicians also concurred.

Dell'Agli M *et al*^[18] as part of a multi-lateral team has reported the *in vitro* anti-plasmodial property of OMARIA against drug resistant strains and other related aspects of the corresponding period.

OMARIA at bolus and hyper bolus repeat doses (apparently) does not deliver an heightened efficacy (drug-dose response). Neither are such type of dosing debilitating, nor do they elicit any contradiction. Continuous small doses seem to deliver therapeutic effect. 72 hours is the window required for 'clearance' of parasites from the peripheral blood. Gametocytes of either sex get killed in 24–36 hours.

Blocks transmission is effective. The Hemo-parasitemia initially dips in the first 24 h, then rises marginally in the next 24 h, and then wanes (data not shown). This is consistent with conventional anti-malarials. 18–24 h, is the time by which the afflicted native returns to normal life and work *i.e.*, becomes clinically asymptomatic. Although OMARIA and artemisinin derivatives are phyto sourced, onset of OMARIA's efficacy in the first 24 h, is slow as compared to Artemisinin. We know that artemisinin alone is highly unstable in gastric phase, even sustained or bolus use fails after 18 h, even against chloroquine sensitive *P. falciparum*. Our considered opinion is that OMARIA even in fractions/sub clinical doses indicate marked clinical effect and physiological response as compared with artemisinin. Whereas, it is well known that artemisinin's engineered derivatives *viz.*, artisunate, artimether, artether, *etc.*, are also much more toxic and expensive[19]. Herein, they are not considered because OMARIA is an at home hand makable product *i.e.* green bio-medicine. And it is very economic.

Table 1

OMARIA therapeutic use summary 1998–2004.

Observed results	Number
No. of cases treated	531
Clinically afflicted at report	531
Cases having history of < 5 episodes per year	176
Cases having history of > 5 episodes per year	355
Cases switched from sllopathy	115
Cases reported contradiction	00
Cases reported side effects	00
Re-affliction within 6 months of OMARIA –C	61
Re-affliction within 1 year of OMARIA –C	76
Re-affliction within 2 years of OMARIA –C	382
Cases who said or felt OMARIA –C is better	501
Partly compliant	11
100 % compliant	512
Pre & post treatment blood slides	150
Infants below 5 years old	42
Child between 5 and 15 old	90
Geriatric stage afflictions (above 60 years old)	17
Cases with confounding therapy.	18
Pregnant & lactating mothers.	Not noted

Note: Post 2004, OMARIA use got a fillip, the number of beneficiaries now exceed 5000.

3.2. Clinical presentation (supporting information)

As compared to patients who have been brought with diarrhea and hypotension, administration of OMARIA leads to bowl formation and stabilization of blood pressure. Again, cases that have been exposed to other alternative medicines, multi drug therapies, to any combination of high potency conventional drugs or indicate resistance to physiological saline infusion, concurrent oral ingestion of OMARIA invariably leads to improvement in liver function, blood pressure, down turn of side-effects, and in general recovery. Methyl alcohol induced hepatic cases are numerous among the tribal sub populations due to adulterated alcohol, as also incidence of chronic hepatic damage- induced hepatitis or jaundice. Oral intake of OMARIA is tolerated better with marked all round improvement. In all categories of malaria

affliction caused pathology, workmen go back to work in 48 h. Clinically, 2 – 70 years of age group first indicated unflinching onset of smooth symptomatic recovery along with wane of myalgia, followed by kill (pathologically determined), clearance and nil-relapse status. Return of thirst, appetite, smooth bowel and GIT function is reported between 36–48 h. This includes known resistant cases who used to get *P. falciparum* infection between 4 – 6 times per year, even after full and complete chloroquine – mefloquine and other combinations. In malariasis, anisocytosis is another aspect of the blood picture. OMARIA therapy downturns anisocytosis, and the erythrocytes regain translucence. Also the white blood cell differential count shows a rapid downturn towards 'total count' normalcy during therapy under 40-fold magnification with regain of crisp and crenate boundaries respectively.

The natives live barefoot off the soil and consume non-sterile food hence are also concurrently infested by gut worms, anemia, bacterial, protozoal infection, obstinate viral diarrhea and chronic infestation of helminths. OMARIA retains efficacy. All such clinical presentations also respond to OMARIA to various degrees. OMARIA treatment is marked by gain in total matured erythrocyte count and in the hemogram; with normal bleeding and normal clotting time. In under weight cases, marginal weight gain is reported after a fortnight. Complete recovery of chronic *P. vivax* cases is also observed. Breathlessness (hypoxia in late brought in and chronic cases), myalgia, fever, general fatigue, sleep disturbance, headache, nausea and idiopathic drug rejection in therapy switch cases *i.e.* allopathic to OMARIA cease in complaint cases.

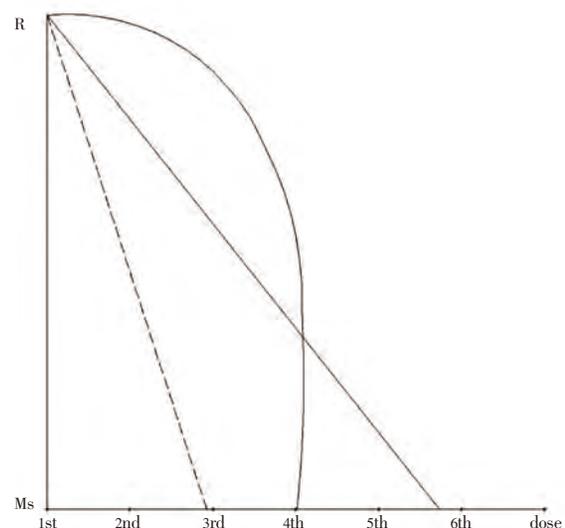


Figure 6. The myalgia-wane schedule suggests anti-inflammatory effect among 100 non confounding cases.

Dotted line – Myalgia; Curved line – Fever; Inclined opaque line – parasitemia.

During the decade, we also noted that the tribal subpopulations when afflicted by any malady complain less about pyrexia (specially the cyclic) and complain more about myalgia. The people of the native tribal are on foot all the while because in the OMARIA use region there are very few roads far and between, neither any public transport system. People cannot remain ambulatory when afflicted by

an ever present pain. Historically, they take analgesics or non steroidal anti-inflammatory as first-aid, including all sorts of barbiturates. On a long period of follow up it became apparent that OMARIA was also being preferred over other medication(s) because it prevent them from myalgia. It was a new clinical finding. We therefore, asked our sample survey questioner to include myalgia aspects as well. It soon became clear that irrespective of the etiology type of the infestations or the status of inflammation, OMARIA was helpful to the native's body ache. This could be due to analgesic effect or a potent anti-inflammatory or either. Figure 6 gives the results of our survey in this direction. It presents myalgia-wane schedule at constant drug and dose in adults of 100 non confounding cases. When blood slides of 42% of the 100 cases were co-related with their statements, we noted that wane of defervescence cycle (being articulated as pyrexia) was slow in registering relief as compared to wane of myalgia *i.e.*, body myalgia waned precipitously from about the second dose of the treatment. These are results without paracetamol /any anti-pyretic/ analgesic drug as adjunct. If paracetamol were administered at 500 mg for each adult concurrently with initial two doses, then representative lines for myalgia and pyrexia and rigor will show very close proximity. This led the author who was also involved in anti-pyrogen/endotoxin technology to write to The Office of the Indian Prime Minister indicating that the original inventor of paracetamol had created it as an anti-inflammatory invention and less as an anti-pyretic. It led to revision in lable of this medicine. However, peripheral blood smear slides shows parasites even post the 48th hour. By such time the native was self determining that she/he is now no more afflicted, which is why they all got to be up and about. In other words, it was myalgia that was indicating a consistent down regulation immediate post the second dose.

On re-examination of the structures of the ellagitannins and their known aspects including selected published *in vitro* data we noted that, our candidate moieties were the sole large carboxyl-hydroxyl group present. They were also acting as 'process scavengers' and are the principle cause of down regulating diffuse, innate inflammation syndrome which is a hall mark of malarial, sepsis and blood dyscrasia. The use of the term 'process scavengers' denotes anti-oxidative role in all conditions of *in vivo* biochemistry. In other words *in vivo*, the alchemical process scavenging is same as biochemical anti-oxidation, clinical anti-inflammation, and pharmacological anti-inflammatory.

During the period of 2004-2005, another 211 cases were also examined with 81 of the previous 100 cases, and 30 of which were re-interviewed as a quick sample survey by a multi-disciplinary team in May-2008 as part of very long term follow up. The report remained consistent. All other current anti-malarials are neither reported nor are clinically observed to down regulate malaria associated diffuse, innate, systemic, spiraling inflammation. We stress on these aspects because successful in-hospital management of inflammation is more than half the battle in status cerebral malarial. Individual feed back along with long term re-validating follow up by revisits and in new cases (till date *i.e.* decadal), has also been consistent and corroborated.

Dell'Agli M *et al*^[20] has reported that OMARIA fails

cerebral malaria via the very potent cum effective route of NF- κ B while down regulating MMP-9 promoter activity. Use of analgesic in status cerebral malarial spells doom. Similarly, if iodine or iodised salt be administered it also spells doom for the afflicted native. Due to the presence of iodine in common salt, severe/systemic malaria develops into cerebral malaria, which in turn progresses to refractile status and eventually to fatality. We further noted that the native takes over doses of common salt post severe bouts of defervescence. Now, a significant portion of the commercially available common salt turned out to be iodised. Our advisory to take rock salt which is known as *saindhava* in Ayurveda or sea salt or salt derived from the back of the cuttle fish (*samudra lavana*) co-linearly with pinches of KCl proved very helpful to the natives across the spectrum. Similarly, when assisted with OMARIA, crisis wanes clinically. OMARIA is a potent anti-inflammatory. Later on we found that iodine was inflicting a liver failure type condition which we will report in subsequent communication.

3.3. Salt processing

What was the need to develop the unique cum atypical thermic process of retreating common salt? We did so because, due to high temperature in sealed, porous (sandy loam), inert container - NaCl's lattice breaks and becomes amorphous, impurities, iodine, and additives are burnt off and get deposited on the inner side of the lid. NaCl gets demineralised, becoming sterile, enriched and separating from all additives. It is ready for use as 'neat-safe', oral restorative. D Bhattacharya^[21] also reported that, ellagitannins, when conjuncted with buffering salts of mono and divalent cations (KCl and NaCl) thwart cerebral malaria and also up-regulate efficacy of the tannins and the tannin spiked moieties. Such salt is not used in prophylaxis. Only dermis powder is used in prophylaxis.

3.4. Fruit stage selection

In nature, methylenation causes fruit to ripe, softening and thinning of the rind along with production of traces of cyanide. By natural selection, our candidate *dalimba* undergoes least methylenation. Which in turn also means thickening of the rind with least to nil production of cyanide, with very low fructose (our data). Which we hypothetically correlated as the cause of it being the historical choice of the Ayurveda. The *bedana* and (to some extent) even the commercial grade Type-2 *dalimba* suffers lack of such natural mechanics and hence has a thin, soft rind with other therapeutics and specially prophylaxis related disadvantages.

The rind of the immature *dalimba* (Type-3) is preferably used at chloroplast stage. At all immature stages the phyto-hormone cascade leading to 1-amino cyclopropane-1-carboxylic acid (ACC) synthesizes and even its precursor, 1-ACC synthase, is in un-evolved state. Therefore, plucking the fruit at such stage does not result in ethylenation of the dermis during pre-process stock-store period, nor when exposed to the sun. Drug moiety yield are best. Such rind

Table 2

The summary of the result of OMARIA as a oral prophylaxis candidate after 1 year. Such prophylaxis was reported and clinically continues to be observed.

Village	Total homes	Total inhabitant	Infant	Child	Adult	Old	Malaria	Measles	C. Pox	Births
Badamput	35	173	6	34	117	10	5	3	–	6
Gunthaguda	26	119	26	21	66	06	–	3	–	2
Mundaguda	27	109	18	25	56	10	–	–	–	4
Total	88	401	50	80	239	26	5*	6	0	12

* Six cases did not avail OMARIA in Badamput village, as they were floating population (non rial group), but were registered residents.

powder is visually rich brown (Figure 7) or else, becomes a shade yellowish, relatively easy to pulverize *i.e.*, more of fine dust is got relatively less sticky–low tannin and low iron content. The phyto–hormone cascade terminates with ethylene (gas) production in the rind. Ethylene synthesis is also collinearly associated with the lysis of the large ellagitannin compounds. These large compounds of the hydroxyl group are long–acting anti–malaria and anti–cerebral malaria candidates, we randomly select at all pre–ripe stages.



Figure 7. The powder of dalimba was filled into gelatin capsule.

Moreover, pre–ripe plucking apart ensuring loaded drug moieties, also precipitously cuts off the supply of the amino acid ‘Methionine’ and results in a downturn in the rate of ripening, or decomposition (black spots) and complete freedom from viral infestation, post pluck. Due to near absence of methionine, its conversion to *s*–adenosyl methionine (SAM) by the enzyme SAM transferase (an intermediate) does not happen. As a result the normal cascade of enzyme → acid → hormone → gas, does not happen. It results in (unusual) hardening of the rind with commensurate preservation of the otherwise susceptible/labile large hydroxyl compounds. Hence, Sun drying in hot tropical condition does not trigger residual ethylenation, nor slow degenerates the principal moieties. They remain within a rind stable envira. Hence, the rind is additionally a candidate for a (hitherto) new plural and rural Bio–medicine.

The rural folks can use it and fight malaria at home.

3.5. Prophylaxis results

Table 2 presents the result of OMARIA as a oral prophylaxis candidate after 1 year. Such prophylaxis was reported and it is being continually observed clinically.

4. Discussion

The above averments are based on ensured actual use by the Red Cross clinic and the District Magistrate’s officials, with annual follow up. Before the usage to the patients, informed consent with left hand thumb impression of patient was taken and address was maintained. This went on till 2004. After 2004, it had to be discontinued. However, the Red Cross clinic/dispensaries maintained register and number. It now shows that more than 15000 cases have been treated by the Red Cross Society using OAMRIA therapy. Prophylactic cases will add up to few hundreds more. Please note that OMARIA was never introduced as a drug trial or having any commercial objectives, neither any industry type mechanics working within or from the hind. Before the treatment, at least 1% of the village’s population required urgent clinical help/hospitalization every fortnight. During the same period and till the date, the neighbouring villages which were not treated reported and continue to report high incidence of Malaria, including cerebral malaria. Individual cases have been and continually followed up for years. There isn’t any indications of resistance to OMARIA. Numerous cases continue to exhibit prophylaxis for years (variation on individual basis). This type of long period observation model was the initial reasons for delaying this report. The finding that OMARIA relieve myalgia and that mere down–regulation of myalgia effected symptomatically gross relief at clinical level posited as additional prime reasons for further delay of this report. Thereafter, the observation that OMARIA blocks transmission and above all fails cerebral malaria became additional causes of delay. We are happy to confirm that OMARIA has turned out to be a “Bottom Up Model” and that long period clinical response is in consonance with the *in vitro* results.

OMARIA is a bio–medicine. It is effective in diverse concurrent non–infestive and concurrent infestive cases of chloroquin sensitive and drug resistant malaria(s), in very challenging, hostile, remote clinical conditions in a long–term basis. it is effective prophylaxis, therapeutics. OMARIA also has compatibility with human physiology, synergic action when it is concurrently used with any other anti–malarial of the conventional or alternative schools of

medicines. clinically do not indicate to pass the blood brain barrier nor the placental, as well as prevent and reverse cerebral malarisis. It is also non analgesic, non anti-pyretic, non muscle relaxant or anything alike. A semi-synthetic and a synthetic are possible.

Large hydroxyl group of ellagitaninns of OMARIA (a) jointly and severally with ellagic acid delivers plasmocidal activity (b) either have process scavenging/anti-oxidative\anti-inflammatory efficacy (c) eminently non-toxic (d) ellagic acts rapidly; has a significant hepatic phase, with short plasma life (e) ellagitanins act slow, at gut phase; have long plasma life (f) between them either have synergetic action and also with other conventional drugs (g) K⁺ act as driver; assists in reversal of cerebral muscular morbidity (h) iodine induces & intensifies refractile pathology; drug failure and liver failure (i) wide spectrum efficacy (j) prophylactic (k) therapeutic (l) prevents & reverses cerebral malarisis (m) apparently, does not pass blood-brain and/or placental barrier (n) Happy to report no emergence of drug resistance.

OMARIA indicates good efficacy on compliance, with slow onset^[22]. It also has a potent use vis-à-vis pathologies and therapies that are associated with diffuse systemic inflammation (acute/chronic). OMARIA (ingredients) apparently posits as a good wide spectrum home remedy. It suggests a paradigm shift among known anti-malarials, world wide. It is an original find (an invention). OMARIA merits further multi-lateral investigation, wider clinical correlation and more evidence based evaluation. Let us 'Fight malaria at home'.

Conflict of interest statement

We declare that we have no conflict of interest.

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