

Orissa Research Indigenous Attempt for Rheumatism and Arthritis: ORIARA

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Abstract

A late mediaeval/early modern period palm leaf (by Panchu Daasa) based lead information is perused and a unique, broad spectrum arthritis related anti-metabolic natural medicament is reported on 2 decade based use cum on-line development. Name: ORIARA (Orissa Research Indigenous Attempt for Rheumatism and Arthritis). A unique starch based keton compound is the active pharmaceutical ingredient. sesquiterpene/eudesmanes viz., Cyperene/Cyperenol, Rotundene/Rotundenol be the APIs. Ground breaking work along with clinical indication. Bottom up model for drug discovery resource personnel.

Keywords: Arthritis; Orissa research indigenous attempt for rheumatism and arthritis; *Cyperus*; Sesquiterpene/eudesmanes, Cyperene/Cyperenol; Rotundene/Rotundenol

Introduction

The Oxford Text Book of Medicine announces arthritis as the “disease of the rich” [1]. Harrison’s limits self to near same description and emphasize the diction ‘metabolic disorder’ [2]. Either, via voluminous renditions wind up silently stressing the frailties of the modern clinician, yielding full defeat. The drug discoverer’s community (God on Earth) alike the master of trapeze have exhausted self and systems executing, visiting and revisiting every trick and track. The gaining ground concept is ‘metabolic etiology’ (back to school). The gamut of clinical signatures are noted to be coalescing as ‘rheumatism’. Our considered view is that arthritis is the signature of catabolism in\ of arthropods. Rheumatism and arthritis are independent. Either are here to stay.

Ayurveda (plural longevity) posits as attractive by such transliteration. Ayurveda is India’s national school of medicine. People trained in the Hippocrates model sneer at it (native Indian specially). In the neighbourhood (author’s home town) is the State (county) level Government Museum, wherein are preserved some 30,000 palm leaf manuscripts ~ covers life and times [3]; some of which are historically ancient. The tome also contain valuable manuscripts pertaining to health care sciences (vet and avian included), and very little is known about the captions and their sterling contents [4].

Now, Ayurveda has invested mind and time on arthritis\rheumatism. Clarionly it announces arthritis as ‘baata’ (sans any deviation or dilution over the historical period of last millennia). The stemma of this phone lies in the vernacular term *vayu\baayu* i.e., ‘wind’. Deepak B immersed self in addressing the systemic winds and gases (including venal) in the patient’s body. Not a single case responded (a resounding blank). In fact, people who had least venal gases and or bowl gases were more acutely arthritic and whereas, juvenile rheumatoid arthritis and or in cases of the acute osteo-arthritis of dual knee joints, had the least (data not provided). Deepak B then digressed into meteorology sciences to acquire an rudimentary understanding about ‘wind’s domain’ (*Vaayu Mandala*). Clearly, ‘baayu’ means and denotes ‘fluid’. The inspiring indications was that ‘baata’ may mean ‘(mal) physiological fluids’, and not as systemic gases. Ayurveda uses the phone pair ‘ganthi baata’ to announce the chapter\ formulae\pharmacognasy) etc. Ganthi is the vernacular phone for joints. Thus, the Oriental expression ‘ganthi baata’ means ‘gone wrong joint fluids’. Fluid seems to be the focus (there are no alternatives to the informed modern drug discovery mind). It is

ancient Oriental technical term for arthritis of the joints. The modern Occidental phone ‘arthritis’ means ‘gone wrong joints’ (osteo seems to be the focus).

Inspiration

Historical and heritage

Deepak B had turned over his ancestral palm leaf manuscripts to the above mentioned museum (a few in the 2 tomes) [5-7]. Rama NP had not in his native village house a few folios were lying strewn (dark, dusty attic). It is authored by Pandit (the erudite) Mr. Panchu Daas, Dt., to between c. 1850-1925 (Figures 1-3). It is written in Odia lingua and script. It is iron stylus engraved, with charcoal black as the contrast providing ink and mentions the captioned malady as ‘*ganthi baata*’ (joint fluids). It is an original member (not a recession). It mentions numerous formulations. One mentions the *Cyperus rotundus* (muthaa) as the major constituent. Novel use indeed. *C. rotundus* is used extensively in ayurveda in ‘n’ number of formulations and for ‘n’ number of clinical conditions (mostly as a minor member). Such exclusive status of *rotundus* vis-à-vis Baata (arthritis) attracted Deepak B attention. From 1993 till 1998, the herb *C. rotundus* (specially) was studied along with the full formulae. The exercise was termed as ORIARA (Orissa Research Indigenous Attempt for Rheumatism and Arthritis).

Cultural and heritage

Asia is home to all the ancient civilization off which the Indian component was there and is alive (in continuum). It is also the land of tradition and culture. Thus, the continent abounds in ancient knowledge some of which have come down to us as texts (a part of which is health sciences). The texts relating to health care within present day India make numerous reference to pain management (possibly 2nd to skin ailments\care). Interestingly, they make numerous scientific averments, note worthy being about the osteologic frame; blood forming hollowed

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Received August 18, 2017; Accepted August 29, 2017; Published September 08, 2017

Citation: Bhattacharya D, Panda RN (2017) Orissa Research Indigenous Attempt for Rheumatism and Arthritis: ORIARA. Transl Med 7: 196. doi:10.4172/2161-1025.1000196

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Figure 1: Is the obverse side of Sri Panchu Daas's Mss.



Figure 2: Is the reverse side of the same folio. Together they give the details of the formula. It is a bit different from that of the Formula indicated in Table 1 (which is indicating high efficacy in present times in all sub-section of the afflicted populace). Original iron stylus engraved Palm Leaf Mass., However they mention *C. rotundus* for the first time as the dominant constituent (enough of a lead to the mind versed in drug discovery art).

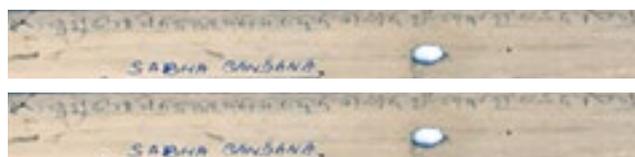


Figure 3: Is that of the terminal/start folio. It is captioned as "Sabha Bandana" (ode to the congress). The full bundle (20+ folios) be the congress. Panchu narrates as to how he had taken his findings/achievements to the Khorda King (Jagapati), who put a deaf ear. Vexed, the erudite Panchu Dasa calls the king as "Hetaa Mundia" (hyna headed). Things have remained more or less the same in India? Think. Folios are in author's personal possession. Details, sharable.

bones (*nalaka*) and the chyle within - are as exact as is modern science [8]. For the frame, they use the term '*asthi*' (stony bones). Cartilages and evolving bones are discounted. Only due modern inquest we do know that bones are CaCO_3 i.e., stone. The question arose what else do the Hindu Indian do? Well, post demise they burn their dead and take a piece of the most stony part of the burnt bones and immerse it in the confluences of the big rivers (namely the most best being the Sangam\prayag at Allahabad, UP {confluence of rivers Ganga and Jamuna}). The question is why? It is symbolic of returning the natural to nature. This is a socio-cultural practice; is history of science wherein is embedded knowledge.

Blood makes bones and bones make blood. Now, the fetus is delivered sans any CaCO_3 stage bones. Even 2 year post partum such status remains. As the being inhales and exhales air the cartilages oxidize and metamorphose into 'asthi' i.e., CaCO_3 is formed (along with blood formation). It is a slow and long process. Therefore, formation of bones is a by-product due the process. Hardening and porosity is sex and age related, respectively. Again, further studies indicated that toxins could be delivered *in vivo* being directed as organ\cell line specific. Toxins could not be delivered to bones. Even the most virulent endotoxin derived from *E.coli* 55:5B or the exotoxin Pot. Cyanide do not effect the osteologic frame [9]. This proved that drug delivery routes to the bones were non-existent (mother seems to cut off the route at labor) including toxins like Methotrexate. Therefore, a candidate had to be looked for which could circumvent such natural baffle. Nature observation indicated that worms are bone less. And, they eat and even grow out of the kernel of the nut grass's rhizome (*cyperus*). This, was alike match stick to gun powder. The ketones (Figures 4 and 5) could probably be uptaken swiftly by the muscles and then to the bones via



Figure 4: *Cyperus rotundus*. Numerous pieces of rhizomes ~: with hairs; removed by mechanical scrubbing; thick black tenacious skin (carp); roots; buff white kernel (unique starch – ORIARA's target candidate), bland-yet tasty; tough; energy giving; that hardens with aging, with air/sun drying; not soluble; on long storage disintegrates from within leaving a hulk under the carp. Worm friendly. Very diff., from tapioca or potato starch.

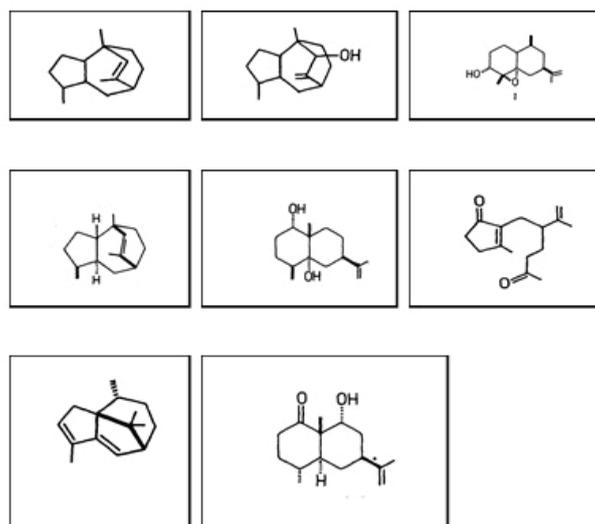


Figure 5: Architecture of the select ketone compounds. Similar. Easy to synthesis. Juvenile *Cyperus* starch when exposed to sesquiterpenic – eudesmane (terpens) undergo interstitial space lysis →harden → smooth with low gloss.

the osteoblast-osteoclast cycle (hypothesis). Decades down since the inception of ORIARA it seems to be working as conceptualized. The time required works out to ~ 60 days, @ 1 gm/day (natural whole), adult, male/female, 60 kg, Asian (lower threshold). Post 300 days of ORIARA therapy DEXASCAN indicates a therapeutic shift (backwards) from osteoporosis zone to osteopenia (average of a 100+ case). Translation medicine stage has well been reached. It is time to open the finding to the glare of more able minds. Drug makers may fjord forward. Social welfare is paramount.

Materials and Methods

From C. 2000 limited public use commenced (challenging clinical cases). Local leading vernacular press carried the information about the new development [10]. Between 2011 and 16 it was licensed for commercial use by the Odisha government and then again by Gujarat government between 2014-16 (3rd parties). All this resulted is the generation of user-feed back based long period data (1992-2016) from patients from across India. And, has an enviable variety of life style, ethnicity, and agro-met conditions (the becausing and controlling factors

of metabolism). Thus, ORIARA got vetted in terms of time and place.

The formulae as in Panchu Daasa's Mss., uses *rotundus* @25% and sucrose 25%. Table 1, is the current innovated formulae (in use). In place of sucrose (nabata) the salty fluid from the upper internode of the sugar cane is advised (concurrent fresh intake). *Saccharum officinarum* Linn (sugar cane) is a perennial grass of *Poaceae* family; native to India\ Orient. The upper internode(s) are full with Xylem tissues in development phase, is loaded with natural glucosamine (minimal reducing sugars). Synthetic glucosamine is physiologically incompatible; is a load for the renal parynchema in the short term and side effects loaded for the nerve systems and the involuntary myard, in the long term. Figures 1 and 2 advises use of whole herbs/constituents; so too do the sole proceeding work [11], which uses the roots of the *Cyperus*. Singh N et al. [11] uses the roots of the *C. rotundas*. They report as anti-inflammatory. ORIARA discarded the roots and used the kernel of the rhizome (Figure 4). ORIARA is immunomodulatory (anti-auto immunity). Interestingly, the said journal does not indicate the full mss., – available only as an special insert\flyer (suspicion arousing). Vis-à-vis the constituents as in Tables 1 and 2. Deepak B selected parts, parcels, studied the bio-chemicals, their therapeutic aspects, contradiction, and used own innovated processes. ORIARA started yielding startling results. Even Govt., of India's official compendiums (regional/county level included) do not allude to any anti-arthritis efficacy of the kernel/extracts of the *cyperus* [12-14] nor do the predating extra Indian authentic publication [15] and or the subsequent works [16].

Figure 4 is live sample, tropical, deciduous, forest, semi laterite, India monsoon period (27-7-17), never exposed to fertilizers, insecticides, etc. pristine conditions. Yet, to flower. API moiety loaded as in Figure 5. Cross section is 1 cm. Noteworthy, human neuron cell type format. Lymphadinopathies also present a similar architecture (specially in metastasis).

Useful (work ongoing)

Singh N et al. [11] uses the roots (not the rhizomes). The root to the viewer's right emanates from the weed supporting rhizome terminates in numerous roots with a brush like ending. The root to the viewer's left as yet has not given germination to any Ariel weed. Yet, it is full grown rhizome. The horizontal spread is 10 inches. Between the two hizomes, the connecting root has thinned. It will eventually lyse and a separate

new weed network shall get to be from the left rhizome. It is a cycle. Oscillating and migrating. ORIARA uses the rhizome.

Process and steps

Availability is season specific. India country side abounds. Constituents are collected, examined, cleaned, washed, dried sun or shade), parts selected, cut to various lengths, size and ground to various mesh and screened separately. Moisture content, aroma/flavor, visual neatness is rechecked. Accurate weighing is done using a standardized balance\volumetric vessels. Ground to 100 mesh, manually filled into '00' size capsules @500 mg\cap for fixed dose therapy, which ranges between 180 days to 300 days. Care is taken to avoid fields exposed pesticides, insecticides and even non-organic fertilizers.

Sterilization

The whole ready mix is treated to 15-20 kilo gray of gamma radiation for total sterilization.

Active pharmaceutical ingredient (API): In Ayurveda the herb is the API. In modern medicine the active principle be the API. Figure 4 is that of the *c. rotundus*. It is a rhizome. Roots emanate from it. The rhizome's body has thick coat of black hairs and a tenacious black coat as carp. The roots and the hairy stalk have contradictory and conflicting effects and also confound. ORIARA clean shaves the rhizome. Inside is starch of buff white colour. It is a unique type. Stable. Compared to tapioca and or rice starch it is more stable, less hygroscopic, almost non-reactive (excellent food for zoonoses; gut worms and flea-fly culture bed material). This is the core starting material (CSM) for isolation, purification exercise-methods and or synthesis (leads). Due to seasonal and agro-meteorological variations the C, H, and O compositions of the CSM varies within a 10-15% range (apart due to process handling soaking period during washing; type of drying; storage thereafter). Also results in a range of chemical formula(s) and architectural forms (non-identical); which is the hall mark of sesquiterpenoids/eudesmanes. Variation in the yield is then more noted for the volatiles (seasonal/agromet/physiography, etc., natural conditions apart). The yielded structures corresponded with the known compounds viz., *Cyperene*/Cyperenol, Rotundene/ Rotundenol; the formula works out as $C_{15}H_{24}O \sim C_{17}H_{26}O_3$ and $C_{20}H_{30}O_3 \sim$ respectively (*Cyperene* being the major); ~400-600 Daltons. Least to nil para-magnetic and or bisabolane type

Sl. No	Botanical Name	Sanskrit / Vernacular Name	Part used	Amount in w/w or v/v as %
1	<i>Linum Usitatissimum linn</i>	Atusi	Wood	3-57
2	Cedrus/deodar (Roxb.) / Polyalthia Longifolia	Devdaaroo	Wood	-do-
3	Corandum Sativum	Dhania	Seed	-do-
4	<i>Corcus sativus linn</i>	Kesura (padma)	Tentacles/pollen	-do-
5	<i>Colocus aromaticus</i>	Kuruveli	Aerials	-do-
6	<i>Piper nigrum linn</i>	Marcha (gol)	Seed	-do-
7	<i>Resua fessea</i>	Nageswara	Flower	-do-
8	<i>Foeniculum vulgare</i>	Panamadhuree	Seed	-do-
9	<i>Trapa lispinasa / loispinosa</i>	Pani Singada	Fruit (aril), carp discarded	-do-
10	<i>Pterocarpus santalinus linn</i>	Rakta Chandan	wood	-do-
11	<i>Pluchea lanceolata (C.B.Lake)</i>	Rasana	Aerials	-do-
12	<i>Hemidesmus Indicus (R.Br.)</i>	Sarba/Ananta Moola	Bark	-do-
13	<i>Asparagus racemosus</i>	Shatavari	Aerials	-do-
14	<i>Curculigo orchioidis</i>	Talamuli	Stem	-do-
15	<i>Cyprus Rotundus</i>	Muthaa	Rhizome	50

Note: *Cyprus* has numerous sub-spp. Spp., *Rotundus*, yields highest; ease of machining; native to Odisha/Odra - moist agro met/riparian conditions (e.g., Prachi\ Orient). Alone inflicts significant anti-arthritis and related metabolic effect. The other constituents have un-putdownable synergistic, adjuvant and specific anti-arthritis roles – making the whole holistic (separate report).

Table 1: Gives our make ORIARA formulae.

Sl. No.	Constituent	Efficacy	Comments
1	Constituents No. 1 to 14 (sans cyperus); whole extracts included.	Moderate	Soothing; refreshing; anti-inflammatory.
2	Cyperus + Natural Glucosamine	High efficacy, in all acute cases; specially in JRA and Deformity	excepting cases of psoriasis and cancer (non-lymph; non leukemias)
3	Cyperus liquid extract (whole)	Rapid action; best in rheumatoid heart. Useful in Leukemias	excepting cases of psoriasis. Rapid mobilization of Ca from muscles to bones requiring oral intake of CaOH = swift normalcy (no muscles cramps).
4	Cyperene/ Cyperenol, Rotundene/ Rotundenol (MeOH extract)	Dose-Therapy drastically reduces.	-do-
5	Cyperus liquid extract (whole) + Penicilin G + Paracetamol	Good	For inflamed and swollen rheums (pain) i.e., (rheumatism); synoviums (septic arth); arthritic hypoventilation; and dilated hearts
6	Cyperus + Colocesia (both rhizomes)	Moderate to good; Complementing and Supplementing	Systemic lupus erythrematous; Muscle wasting; etc., related
Note i	ORIARA therapy leads to mild muscles cramps due to mobilization of Ca from muscles to bones oral intake of CaOH = swift normalcy (elemental Ca is not comparable; neither as safe).		
Note ii	At atomic level the drug design concept is Electron donation. Proton trapping.		

Table 2: Other formulas.

property. These are ketons and be the APIs (full of opportunity). Figure 5 is the cyperene/rotundene skeletons.

Applications of API: The APIs have the following applications (Table 3).

Cancer vs. arthritis

Deepak B was concurrently also involved with bench-to-bed medicine (Translational) in the domain of Malaria [17] and Cancer [18]. This brought in valuable comparative expouser based education (knowledge). Methotrexate (amethopterin/ $C_{20}H_{22}N_8O_5$) is a chemotherapy compound that is also potent as immune system suppressant. In India there is a new craze to use this to treat arthritis (proving deleterious); west likely to denounce. Arthritis is very different from cancer. The sesquiterpene/eudesmanes viz., Cyperene/ Cyperenol, Rotundene/Rotundenol mostly have only C and H molecules. O is low. N is absent. Furthermore, these compounds mostly have venial proton. In the studies related to anti-meatastasis/ anti cancer (ATAMCOX) we have used electron depleted item as the candidate and have used proton donation concept. Thus, right from the beginning ORIARA was designed (to the opposite/reverse atomic flow) on the platform of electron donation with low or anti-proton candidates (arthritic joint have low energy {i.e., energy inefficient} fluids; cancer edema are energy efficient fluids). The decade ++ period field observation is that telephone line men keep getting exposed to low voltage direct current shocks. Non seem to suffer osteo-arthritis (or require joint replacement)! Electron beam therapy and/or DC low voltage therapy at sub-clinical dose/s posits as titillating – as a fall out of ORIARA. Proton beam therapy is likely to aggravate (γ and X rays included). Therefore, it would be profitable to study personnel who all are exposed to baryons (Hadron group) from arthritis and or rheumatoid heart\valve affliction aspects.

Results

ORIARA has a history of two decade long clinical observation which in brief are as follows. Ketone – eudesmene – principal active moiety is uptaken via urolithin pathway – mid gut. It is most effective in juvenile rheumatoid arthritis. The efficacy in all other types and sub-types chronologically may be laid out as : anti osteo-arthritis; anti gout; anti osteomalatia; anti-osteoporosis; increases bone density (DEXASCAN evidenced); nourishes bone marrow (hemogram normalcy restorer); nourishes bone joints (all types); maintains and restores synovium

Applications of The APIs	
Clinical Presentations Most effective	Juvenile rheumatoid arthritis. osteo-arthritis; gout; osteomalatia; osteoporosis; bone re-mineralisation; nourishes bone marrow (hemogram normalcy restorer); nourishes bone joints; maintains and restores synovium membrane (deformity is restored); maintains and restores synovial fluids; pannus cells architecture regain; frozen shoulder; diabetes; heart valves; blood vessels, hemodynamics; rheumatoid heart; anti-inflammatory; hot flush; anti-reactive oxygen species generator; brown adipose tissues; renal incontinence; dilated hearts; arthritic hypoventilation; Systemic lupus erythrematous; Muscle wasting; etc., myard and connective tissue related. Etc.
Pharmaceutical Aspects High points	Moderate; High efficacy, in all acute cases; specially in JRA and Deformity; Rapid action; best in rheumatoid heart. Useful in Leukemias; Dose-Therapy drastically reduces. Moderate to Good; Complementing and Supplementing; uptaken via urolithin pathway – mid gut. 90% liver metabolized. Driver potential (receptor) - para-magnetic and or collating bisabolane type property.
Collateral Clinical Matters	Soothing; refreshing; anti-inflammatory; Excepting cases of psoriasis and cancer (non lymph; non leukemias). Rapid mobilization of Ca from muscles to bones requiring oral intake of CaOH = swift normalcy (no muscles cramps). For inflamed and swollen rheums (pain) i.e., (rheumatism); synoviums (septic arth); idiopathic - non anemia weight loss.

Table 3: Applications of API.

membrane (deformity is restored); maintains and restores synovial fluids; maintains and restores pannus cells (regain load bearing); frozen shoulder; helpful also for diabetes (reduces post prandial) and obese persons; salutary effect on heart; valves; blood vessels, also on hemodynamics (normaliser); high efficacy in rheumatoid heart; anti-inflammatory; anti hot flush; anti-reactive oxygen species generator; salutary effect on adiposes – specially the brown adipose tissues; reduces BMI (reduces flab; tightens in women). Arthritis is also associated with

(male) renal incontinence etc. ORIARA proves useful.

Non-anti spasmotic (gut); non-muscle relaxant; non-teratogenic; non-psychosomatic; non sedative; non hypnotic; non-sleep inducer; non-anti-pyretic; non pro-pyretic; does not pass the blood brain barrier; non-energy inducer; safe in pregnancy (observed in JRA + pregnancy = safe, sound delivery, with mother correction of deformed joints of the mother); pediatric use. Salutory effect on adiposes – specially the brown adipose tissues. Reduces BMI (reduces flab; tightens in women); etc.

Contra indications

Constituents No. 1 to 14 when used as a formulation (post blending) also indicate mild to good anti-arthritis efficacy. Constituent No.15 (*C.rotundus*) alone indicates high efficacy (H₂O/MeOH/Alcohol). However, the *Cyperus* is gut worm and pore friendly (need periodic cleansing). It is contradictory in psoriasis, all types and forms of necrolytic skin conditions and in tumor, cancer and carcinomas. The roots and carp of the *Cyperus* are pugnacious, light-voluminous, baffles during tablet/capsule engineering, infection friendly, and has very low therapeutic effect, save and except that it seems to have some down turning effect on drug induced pruritus, ictirus and psoriasis (investigation on).

Discussion

The rhizome of the *Cyperus* is a nut. Neat kernel is safe, good food. The Ariel part is a tenacious weed. The government of India in all its agricultural departments and branches consider this weed as nuisance that down regulates crop yield. *Cyperus* also mobilizes fertilizers away from crop roots and also neutralises toxins (own data). However, *Cyperus* rejuvenates self and soil, annually. In Ayurveda classical texts the rhizome has been a versatile medicinal item at least since 2000 yrs before present. Medicinal herbs do not attract the attention of the modern and the most (fiscally) enabled drug discovery resource personnel. Poly herbals the more (alike ORIARA). Specially due to opposition by allopathy school of medicine (market share controller). In-fact, Ayurveda (the Indian National School of Medicine) is looked down upon by native allopaths and their official professional bodies (also are debarred from advising !); 99% of Asian allopathy practitioners are non Ph.Ds., (70% of indo allopaths are 'under graduates as per USMLE ?). Whereas, such school of practitioners stand at the apex of the health care pyramid. They serve 60% of the 1.3 billion people. They should be allowed to adopt and advice indo ayurvedic modern science based products as different from classical Ayurvedic medicaments (else, national and social loss; down turned family welfare) as complementing and supplementing items. Industry will gain. Herbs are here. They shall stay. Mother nature won't stop teaching. All such aspects have remained untold. We shall try to present numerous aspects (of such unique ORIARA) in our follow up communication (original, ground breaking and pharmaceutically relevant). ORIARA is a nut-food-drug (reverse reading valid). ORIARA is a mission.

ORIARA has 15 constituents. Each constituent has around three active principle from caption context. This makes up to 40-50 compounds. Therefore, we have conceptualized a unique Nano tech based wafer tablet wherein as many compounds can be embedded and a small pill can be made with [19]. Using science and technology to mimic mother nature is the way forward. A salutation to Sri Panchu Daasa.

Conclusion

ORIARA is a mere concept based attempt. It is a bottom up model. The *Cyperus* (and specially *rotundus spp.*) posits as immediate

panacea for arthritis. The sesquiterpenoids/eudesmanes ketones are the candidates for allopathic drug development. Non toxic (actually, anti-toxin). Each and every moiety posit as Translational Medicine. Let the global community make ORIARA and effect patient centric family welfare. The formula in Table 1 can be copied with assured good profit. There are No patents (attempted – turned down after 5 yrs by The Patent Gen of India). Hence, no limitations. No hidden uncatenates.

Acknowledgement

Dedicated to friend Mr. Yogesh Paliwal, Yavatmal, MH for his Rs. 3 Lacs grant. It enabled perusal of the idea ORIARA (for most part it was free given to hundreds ranging over 2 decades). Special Thanks to Prof. Enrica; Prof. Mario del Agli, Prof Tarameli and others (Italy) – for having created space and time for Deepak B (2006-2010) to peruse mission ORIARA. Even initial primary reporting got delayed due to false, frivolous and orchestrated criminal cases (rape and murder) filed against Deepak B by Swapna/Annapurna Chakraborty; Lipika Chakraborty, assisted by Basanti Bhattacharya, Arundhuti Bhattacharya w/o Debashis (AMC-IA); Subhasis Bhattacharya; Susmita Bhattacharya; Vijaya Chakraborty (IFFCO), involving my father and mother; Tacitly supported by Pradip Bhattacharya (RBI); ulterior motive, malafide intentions. Sinister designs. All proven wrong. Police and Judges assisted. God's best are humans on earth.

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