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 (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 stigma 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 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

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 avertments, note worthy being about the osteologic frame; blood forming hollowed

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oxidize and metamorphose into ‘asthi’ i.e., CaCo3 is formed (along with status remains. As the being inhales and exhales air the cartilages delivered sans any CaCo 3 stage bones. Even 2 year post partum such knowledge.
is a socio-cultural practice; is history of science wherein is embedded question is why? It is symbolic of returning the natural to nature. This prayag at Allahabad, UP {confluence of rivers Ganga and Jamuna}). The confluences of the big rivers (namely the most best being the Sangam\nalaka
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 CaCo3 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 CaCo3 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., CaCo3 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 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 Odisa 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 Daas’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 intenode 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 intenode(s) are full with Xylem tissues in development phase, is loaded with natural glucosamine (minimal reducing sugars).

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Useful (work ongoing)

Singh N et al. [11] uses the roots (not the rhizomes). The root to the viewer’s left as yet has not given germination to any Ariel weed. Yet, it is full grown in numerous roots with a brush like ending. The root to the viewer’s left emanates from the weed supporting rhizome terminates 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 insertatory (suspicion arousing). Vis-à-vis the constituents as in Tables 1 and 2. Deepak B selected parts, parcels, studied the biochemicals, 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, yet, to flower. API moiety loaded in Tables 1 and 2.

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 hallmark of sesquiterpenoids/eudesmanes. Variation in the yield is then more noted for the volatiles (seasonal/agromet/physiology, etc., natural conditions apart). The yielded structures corresponded with the known compounds viz., Cyperene/ Cyperonel, Rotundene/ Rotundenol; the formula works out as C₇H₁₀O₂ ~ C₁₇H₂₆O₃ ~ 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      | Linum Usitatissimum linn | Alusi | Wood | 3-57 |
| 2      | Cedrus/deodar (Roxb.) / Polyalthia Longifolia | Devdaaroo | Wood | <0 |
| 3      | Corundum Sativum | Dhania | Seed | <0 |
| 4      | Corcus sativus linn | Kesura (padma) | Tentacles/pollen | <0 |
| 5      | Colocous aromaticus | Kurveli | Aerials | <0 |
| 6      | Piper nigrum linn | Marcha (gol) | Seed | <0 |
| 7      | Resua fassa | Nageswara | Flower | <0 |
| 8      | Foenulum vulgar | Panamudhuree | Seed | <0 |
| 9      | Trapa ipinasa / krapinosa | Panil Singada | Fruit (ari), carp discarded | <0 |
| 10     | Pterocarpus santalinus linn | Rakta Chandan | wood | <0 |
| 11     | Phulus lanceolata (C.B.Lake) | Rasana | Aerials | <0 |
| 12     | Hemidesmus Indicus (R.Br.) | Sarbal/Ananta Moola | Bark | <0 |
| 13     | Asparagus racemamus | Shatavari | Aerials | <0 |
| 14     | Curculigo orthoidis | Talamului | Stem | <0 |
| 15     | Cyprus Rotundus | Muthaa | Rhizome | 50 |

Note: Cyperus has numerous sub-spp. Spp., Rotundus, yields highest; ease of machining; native to Odisha/Odra - moist agro metrinarion conditions (e.g., Prachil. Orient). Alone inflict significant anti-arthritic and related metabolic effect. The other constituents have un-potdownable synergistic, adjuvant and specific anti-arthritis roles – making the whole holistic (separate report).

Table 1: Gives our make ORIARA formulae.
property. These are ketones 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 exposurer based education (knowledge). Methotrexate (amethopterin/C₃₈H₃₁N₇O₉) is a chemotherapay 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 in brief are as follows. Ketone – eudesmene – principal active moiety is uptake 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 membrane (deformity is restored); maintains and restores synovial fluids; maintains and restores pannus cells (regain load bearing); nourishes bone marrow (hemogram normalcy restorer); (non-lymph; non leukemias)

| 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 |
| 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. | - |
| 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; |

**Table 2:** Other formulas.

| Sl. No. | Constituent | Efficacy | Comments |
|---------|-------------|----------|----------|
| 1       | Cyperus 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 |
| 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. | - |
| 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; |

**Applications of The APIs**

| Sl. No. | Constituent | Efficacy | Comments |
|---------|-------------|----------|----------|
| 1       | Cyperus 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 |
| 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. | - |
| 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; |

**Table 3:** Applications of API.
(male) renal incontinence etc. ORIARA proves useful.

Non-anti spasmodic (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. Salutary effect on adiposés – 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 necrolyting 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, icitus 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 herals 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-gen of India). Hence, no limitations. No hidden uncenates.

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