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The efficacy of Kusthaghna Mahakasaya & Takradhara in the management of the Psoriasis (Kitibha)-A Clinical study.

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ABSTRACT

Psoriasis is an immune mediated genetically determined common dermatological problem which affects skin, nail, joints flexures and folders of the body. There are lots of treatments available for Psoriasis but due to its relapsing nature psoriasis is challenge to treat. Today's medical science treats this disease with PUVA and corticosteroids but this type of therapy has serious adverse effect on many vital organs like liver, kidney and bone marrow. On contrary to that Ayurveda has some very effective remedies for psoriasis (Kitibha), provides long lasting results and a better life to the patient through its unique fundamentals. Medicine like Kusthaghana Mahakasaya and Takra has a very good response over that disease. So I have selected both the medicine to conduct my study.

INTRODUCTION

All the skin disease in Ayurveda has been described under the board heading of kustha. There are two types of kustha in Ayurveda. Mahakustha and Kshudra Kustha. Kitibha belongs to kshudrakustha. From the characteristic features Kitibha can be compared with the disease psoriasis of modern medical science.

Psoriasis is a chronic, recurrent inflammatory disease of the skin of unknown origin, characterized by well circumscribed erythromatous dry plaques of various sizes, covered with mica like scales i.e. silvery scales. The main abnormality in Psoriasis s increased epidermal proliferation due to excessive division of cells in the basal layers and a shortened cell cycle time.

PSORIASIS (KITIBHA) IN AYURVEDA

Great sage Charak in Charak Samhita, Chikitsa, 7th chapter 22nd sloka said regarding Psoriasis that Kitibha (Psoriasis) is characterized by-

- Shayava: Bluish-black discolouration of skin.
- Kina sparsha, Rudhavranasthan – Surface of the lesion is coarse like healed wound.
- Khara Sparsha – Lesions are coarse or crough to touch.
- Parusha – Dry lesion

The comparable description is obtainable in Bhavaprakash, Madhav Nidana & Yoga Ratnakar. Astanga Hridaya has merged some more lakshana –

- Kandu – Itching
- Ashitam – Shyavavarna

According to Vagbhatta:

Kitibha kustha has dry skin, is rough and hard, creating sound and Scratching, severely itching, is hard and black in colour

TRIGGERING FACTORS:

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Skin Trauma such as:

- Acupuncture
- Bites
- Bruises
- Burns
- Chemical irritation etc aggravates the condition of Psoriasis.

SEASONAL VARIATION:

The majority patients (89% in one study) experience worsening of their skin lesions throughout winter.

PREGNANCY:

Psoriasis may remit during the time of pregnancy. Rarely, generalized pustular psoriasis may be precipitated during pregnancy most likely due to increased levels of progesterone at the latter half of pregnancy.

EMOTIONAL STRESS:

Psoriasis is quite 'sensitive' than many other skin diseases. Lots of hectic events of daily life may aggravate psoriasis. The diseases itself can cause a reactive depression in the patient, which could promote the deterioration of psoriasis.

DRUGS THAT EXACERBATE PSORIASIS:

Numerous drugs can aggravate psoriasis. Beta adrenoreceptor blocking drugs like propranolol, metoprolol etc. induce a papulosquamous eruption that resembles psoriasis.

Contrary to popular belief and some early unreliable reports, nonsteroidal anti-inflammatory drugs (NSAIDs), salicylates, meclofenaate, phenylbutazoneand ibuprofen, which are commonly used in orthopedics and surgery, have not been reported to either precipitate or exacerbate psoriasis.

CLASSIFICATION:

Psoriasis can be clinically classified as follows:

1. Guttate psoriasis.
2. Chronic plaque psoriasis.
3. Exfoliative psoriasis.
4. Pustular psoriasis.
5. Psoriasis unguis.
6. Arthopathic psoriasis.

MATERIALS AND METHODS

1. Source of Data:

The Clinical study was conducted at Kayachikitsa OPD and IPD at Govt. Ayurvedic College & Hospital, Guwahati, Assam, India.

2. Method of Collection Data:

Study will be carry out on the patients diagnosed as suffering from Kitibha in the age group 10-65 irrespective of sex, religion economic status and occupation.

The total numbers of patient taken for study were 128. Out of 128 patients, 28 patients dropped out. Duration of the treatment was 45days. The patients selected for study were divided into 2 groups as Group A and Group B.

The inclusion of the two patients in these two groups was done randomly. In both the groups Kusthaghna Mahakasaya was given uniformly. However in the group B, Takradhara was given in addition to the Kusthaghna Mahakasaya. The selected patients were interviewed along with their family members and relatives to obtain detailed information about the patient as well as the disease and collected indifferent data along with previous medication and investigation.

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Criteria for selection of patient:

a) Inclusion Criteria:
   i) Patient between age group of 10-65 years.
   ii) The patient having cardinal symptom of psoriasis like erythematous papules/plaques covered with dry brittle, silvery, grayish white micaceaous scale, Auspitz sign, Kobner phenomenon, Candle grease sign etc.

b) Exclusion Criteria:
   i) Patient beyond the age group 10-65 years means below 10 years and over 65 years.
   ii) Patient suffering from other systemic diseases like cancer, AIDS, Diabetes, TB etc.
   iii) Patient having other skin disease.
   iv) Pregnant lady

3. **Study Designs:** Open Trial
4. **Drug:**
   i) Kusthaghna Mahakasaya in Kwath (Decoction) form
   ii) Takra in dhara form.

Selection of the drug:

Kusthaghna Mahakasaya is an indigenous drug. It is mentioned in Charak Samhita, Sutra Sthan chapter 4/92. The ingredients have properties like-kusthaghna, kandughna, vishaghna, raktasodhanetc as described in previous chapter of trial drug review advocated by various Ayurvedic classic and Nighantus.

Preparation of the drugs:

Kusthaghna Mahakasaya is composed with 10 drugs viz. Khadir, Amlaki, Haritaki, Vidanga, Jati, Saptaparni, Haridra, Karavir, Bhallatak and Aragvadh. Out of these ten drugs, two drugs Bhallatak and Karavira was not included in my trial drug since both the drug has toxic effect over the body as mentioned in Ayurvedic classics.

The ingredients were collected and dried in shades. The drug was prepared in Yabakutchurna form and packed 200gm each packet and supplied to the patients. Patients were taught how to prepare the decoction by adding 320 ml of water in 40gm of crude drug and thereafter asked the patient to boil up to the reduction of 80 ml (1/4th of the total water) then filtered. After filtering he/she was advised to take 40 ml twice daily after food.

Preparation of Takra:

Curd was churned first and thereafter water was added and then again that was churned.

Application Of Takra :

Takra was introduced to the patient in dhara form over the affected part and the head for 15 minutes in each and every area initially for 15 consecutive days and continued up to 45 days.

RESULTS

The study evoked the following findings-

1. The age of onset of this disease was high in fourth decade of life i.e. 30-40 age group (40%).
2. The male (68%) were more affected than the female.
3. Maximum number of patients belongs to middle class family (69%).
4. Non-vegetarian (86%) with incompatible food stuffs is more prone

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to have the disease than vegetarian (14%).

5. Maximum number of patients belongs to urban area (75%).
6. Hereditary relation was found in Kitibha is about 4%.
7. Maximum incidence was observed in patients with duration of illness more than 5 years(40%) followed by 3-5 years (30%) indicating the chronic and relapsing nature of the disease.
8. The disease psoriasis is found to aggravate during winter season in 71%of patients.

Psychogenic factor (30%) was found more common followed by infection and physical trauma as triggering factor in initiating psoriasis.

Effect of treatment in terms of complete relief, partial relief and no relief in group A

Result	No. of Patient	Percentage (%)
Complete relief	11	22%
Moderate relief	31	62%
Mild relief	8	16%
No relief	0	0%
Total	50	100%

Effect of treatment in terms of complete relief, partial relief and no relief in group B

Result	No. of Patient	Percentage (%)
Complete relief	18	36%
Moderate relief	26	52%
Mild relief	6	12%
No relief	0	0%
Total	50	100%

DISCUSSION

After the complete study which includes total 45 days, it was observed that patient obtained relief after treatment with Trial drug. Improvement of the patient based on mainly three factors i.e. itching, scaling and Erythema and it was found that indigenous drug Kusthaghna Mahaksaya was able to improve the clinical symptoms of the patient to a greater extent. The reason might be due to the antimicrobial, anti-inflammatory, anti-proliferative and Keratolytic action of the trial drug. In group B, Takradhara externally along with Kusthaghna mahakasaya was introduced orally. Statistical analysis showed the improvement was more in controlling sign and symptoms especially in itching, scaling and erythema.

As more differences have been observed in group "B", the effect of drug Kusthaghna Mahakasaya orally and Takradhara externally is better than only Kusthaghna Mahakasaya orally alone in group A, statistically as far as itching, scaling and erythema is concerned.

CONCLUSION

Thus it can be concluded that the trial drug Kusthaghna Mahaksaya and Takradhara is safe, simple, easily available cost effective therapy to relieve the agonizing patients of Psoriasis.

Further, no adverse effect was observed in any of the Patients and overall therapeutic response was highly encouraging.

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New scope of Bioinformatics can design food and improve health

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ABSTRACT

Million people and animal in the world do not have nourished food. Malnutrition in all its forms increases the risk of disease and early death. Nutritional science can helpful to understand the molecular mechanisms which give heterogeneous responses to nutrient intake, and it can observe in healthy adults. Nutrition scientists are collecting knowledge by merging different fields. There is a lot of information about genomics and proteomics. Now, the emphasis on nutrient search, similar compound search, disease factor and to find a mall nutrition reason. In future we will be capable to analyze mall nutritional changes on DNA and functional disturbance and its recovery method. The aim of this paper is to search beneficial or harmful compound for food. Which affects nutrition.

INTRODUCTION

A good nutrition is a fundamental state for the adults' well being and health. This is also essential for the healthy growth of children. All nutrition errors can increase the risks of many types of Cancers. Low income countries, inadequate amounts of food (causing conditions such as child malnutrition and retarded growth) and inadequate diversity of food (causing deficiency of vital micronutrients such as vitamins, minerals or trace elements) continue to be priority health problems. Nutritional deficiency affects all age groups, but it is especially common among poor people and those with inadequate access to health education, clean water and good sanitation. We suffer from these diseases as a result of the way we live. Many diseases are caused by Malnutrition. Malnutrition describes a partial or absolute deficiency of one or more of the essential nutrients, vitamins or minerals. There is a basic problem in the earliest stages of target selection between the desire to study targets that already have a good-understood role in disease and the desire to study those that might offer a completely novel mode of action. Ideally, Bioinformatics should provide the bridge that reconciles these goals, primarily by providing as many clues as possible to function and role. In target selection In addition to better filtration of targets in early discovery, Bioinformatics can also help with three aspects of target selection:

• The characterization of targets, such as the classification and sub classification of protein families and gene.

• The understanding of targets, such as their behavior in a larger biochemical and/or cellular context.

• The development of targets, such as making predictions about uptake or reuptake, detoxification, the stratification of patient populations and other gene-based variations (1).

Bioinformatics, the discovery process and its computational cycles can be linked to a biological one, such that predictions from the former can be immediately tested at the bench, with the results being fed back for producing refinements of the model. Instead of simply handing candidate genes to an independent bench validation process. In this way, Bioinformatics can add more value by shortening cycle times. Value can also be added to targets already in development by continuing the search for homolog's, both orthologs (homologs in different species, presumed to have a similar function) and paraloges (homologs in the same species, which might have diverged in function), that could provide additional models in other species and follow-on targets that can use existing assays and compound libraries. Genomics has undergone a transition from structural analysis of the genome to functional analysis of the genome, but this joint knowledge can help to find nutritional disease. This information we can merge with Bioinformatics and nutrition has embraced genomics as a source of nutritional compound targets and, as a corollary, has recognized that bioinformatics is crucial to exploiting data produced on a genome-wide scale. There are many benefits of this study.

1. Help to remove malnutrition

Herbs contain unique anti-oxidants, essential oils, vitamins, phyto-sterols and many other plants derived nutrient substances, which help to remove malnutrition.

2. Help to remove disease

Herbs contain anti-oxidants, antimicrobial, antifungal and antiviral compounds. Which help equip our body to fight against germs, toxins and to boost immunity level. (2-9), antitoxic or immune modulatory effects (10).

3. Herb as a source of desire compound

The body needs different compounds such as vitamins, mineral, amino acid and fatty acid, etc. so herbs can fulfill the nutrient compounds.

4. Herbal antibiotic property

Herbal feed additive could either influence feeding pattern or influence the growth of favorable microorganism in the rumen or stimulate the secretion of various digestive enzyme, which in turn may improve the efficient utilization of nutrient, result in improved production and reproductive performance of animals. Harbals are not harmful to the body (11).

5. Shrink uses of Chemical medicine

We usually take chemical compound as a source of preservative, medicine, etc. but its long impact on molecular basis, we can study by Bioinformatics and we can search other alternative by quick study.

6. Essential oils

Essential oils retain considerable popular use of alternative medicine (12). Studies have

shown that certain essential oils may have the ability to prevent the transmission of any drug-resistant strains of pathogen. Taken by mouth, many essential oils can be dangerous in high concentrations. Its effects begin with a burning feel with saliva. In the stomach, the effect is carminative, relaxing the gastric sphincter and encouraging eructation (belching). Further down the gut, the effect typically is antispasmodic. Typical ingredients for such applications include eucalyptus oils, menthol, capsaicin, anise and camphor. Some essential oils act as locally anesthetic counter irritants and, thereby, exert an antitussive effect. Some essential oils, are valued for their diuretic effects with relatively recent concerns about the overuse of antibacterial agents, many essential oils have seen resurgence in off-label use for such properties and are being examined for this use clinically.

Probiotic genetic mode of action

Probiotics, are recently termed as direct fed microbial (DFM) have diversified use in domesticated animals (like small and large ruminants, pig and poultry) and in human beings (13-15). Different probiotics like bacteria, yeast, and fungi are used for manipulating rumen fermentation and the microbial eco-system of the gastro-intestinal tract of animals, to harvest maximum energy from the feed fed to the animals. These probiotics produce secondary compounds which may helpful or harmful for growth. We can dock these entire secondary compounds and search its mode of action and its alternative compound in nature.

New nutrition, enhancing compound research

We can search new nutrition, enhancing compound by docking, which may help to improve digestion, and trigger nutritional deficiencies. This study can be cheap, easy, helpful and capable to search wide area.

Computational methods molecular dynamics and molecular docking have contributed a lot for identification of proteins (16) it becomes more crucial than ever to emphasize the integration of these various knowledge sources for functional prediction the entire drug discovery process.

Table 1. Herbal compound searched by bioinformatics method.

Enzyme / Gene/DNA	**Source**	**Best treated Compound**	**Ref.**
Cytochrome P450 mono-oxygenases (2UUQ) enzyme	*Mycobacterium tuberculosis*	ZINC00004165 (5-[3-(2-nitroimidazol-1-yl) propyl] phenanthridine)	(17)
Rv2623	*Mycobacterium tuberculosis*	Naringin from citrus fruit	(18)
NS3 protease enzyme	Dengue virus	Azadirachtin	(19)
Methenyl-Tetrahydromethanopterin Enzyme	*Methanobrevibacter Ruminantium*	δ-Viniferin, Diosmin and Eriocitrin	(20)
FAT10 gene	Hepatic Carcinoma	Artonin E from the bark of Artocarpus gomezianus Wall	(21)
poly (dA-dT)12 and poly (dG-dC)12 DNA.	Cancer	Anthocyanins	(22)
VCA0739 (YZ39_VIBCH)	*Vibrio cholerae*	Chicoric acid	(23)
NADP oxidoreductase enzyme	*Methanobrevibacter smithii*	Lovastatin and Compactin (Mevastatin)	(24)
3-methyladenine DNA glycosylase enzyme	*Streptococcus sanguinis*	EDA (3- [2-Deoxyribofuranosyl] - 3H- 1, 3, 4, 5A, 8-Pentaaza- Asindacene-5-monophosphate) from 1F4R	(25)
H1N1 virus	Influenza A virus	Hesperidin & Narirutin	(26)
Nudix Enzymes	*Streprococcus pneumonia* (2B06) and *Enterococcus faecalis*	AMPCPR and CID14258187	(27-29)
Collagen-like peptide	*Human*	Naringin and Hypericin	(30)
12bp DNA $(CGCGAATTCGCG)_2$	*1BNA*	Osmium Compounds	(31)

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Short notes for state of art computational methods for Drug Discovery

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ABSTRACT

Structural genomics projects have determined 3D structures of the proteins via high-throughput methods like structure modeling, threading as well as combination of experimental and modeling approaches. These state of art methods help in fast prediction of protein structures which help in finding new drug targets. In addition, ligand prediction methods added extra advantage to discover and characterize new drugs. Here, a small notes are produced to summarize the recent method used for drug discovery programs.

INTRODUCTION

STRUCTURE AND FUNCTION PREDICTION

Structure alignments based methods have been developed to determine the putative functional sites and ligands for Structure genomics unknown function (SG) proteins where sequence homologies have failed. Several state of art methods have been used to determine structure and function of many of these proteins (1,2) such as the 3DLigandSite (3) method employs the principle of finding structure homology for the target query proteins on the basis of bound ligands. Here, the superposition between the structures of known proteins-ligand complexes with the input target modeled protein structure detects conservation of the function sites at the ligand binding pocket. The Profunc server (4,5) determines the function and functional sites annotation for unknown function proteins whose 3D structure are known. It predicts functional relevance based on sequence scanning against the database of patterns or motifs secondary structure elements similarity, like folds, with a database of known structures. Additionally, the 3D templates search (6) employs the finding of enzyme active sites, ligand-binding sites, DNA-binding sites and 'reverse' template residues similarity. However, ProFunc server produces large number of hits for sites prediction with more false positive results.

Other structure-structure superposition methods like DALI (7), detect structure superposition between query SG protein and protein structure database but fail to obtain information of putative functional sites in SG targets. The SUMO server (8) detects the ligand binding sites for the unknown function protein via 3D structure matching. Here, either structure of the query proteins search against the database of ligand binding sites of known proteins or 3D sites from query proteins search against the protein 3D structure for putative ligand binding sites prediction. The PINTS method (9) employs the substructure comparison of amino acid residues which are common to two set of coordinates and

geometrically similar. The similarity among the atoms of amino acids is measured by calculating the scoring analysis of root-mean-square deviation (RMSD) for two sets of coordinates. Docking based method like Q site finder (10) employs energy based criteria to predict the functional or ligand binding sites in proteins. The algorithm is based on the docking of the ligand probe with the proteins and generation of interaction energies. The predicted sites are ranked based on energies and volume.

LIGAND PREDICTION AND CHARACTERIZATION

The structure based ligand prediction methods have been used in drug design and substrate prediction for enzymes. Docking methods have been developed to predict ligand molecules, like FPOCKET, which determines the binding site for putative drug compounds or substrate binding sites for proteins of interest software's such as DOCK4.0 & GROMACS,TINKER, AMBER and NAMD for Molecular Dynamics (MD) (11-13) and PATCHDOCK (14-17) have been employed for putative ligand prediction. Software's like AUTODOCK (18-23) ,GEMDOCK(24) are enabled to perform docking simulation for large compounds dataset against protein targets. These are much faster and optimized for scoring functions. Therefore, extensive use of AUTODOCK and GEMDOCK has been found docking research work. Ligand databases have been developed to find commercially available compounds, natural compounds, cell metabolites as well as known drugs like compounds. ZINC database contains over 20 millions commercially available chemical compounds deposited by companies for computational virtual screening. Another database, PUBCHEM is a public domain database, which includes characterized and un-cauterized chemical compounds, organic compounds with their biological activities, substance description, as well as bioassay information. KEGG ligand database contains information about the chemical substances as well as metabolites of the cellular system and their associated reactions where they are involving (25). Many quantum mechanical (QM) methods DFT, MP2, CC2 etc. have been developed over the years. For optimizing the geometry of a molecule and calculating its properties, such as its vibrational spectrum, each method and basis set combination has its own figures of merit. GAUSSIAN (26,27) is one of the best software which is widely used for characterization of the ligands and their structures.

CONCLUSION

Combination of computational methods such as AUTODOCK, GEMDOCK, PATCHDOCK, GAUSSIAN, GROMACS, AMBER, NAMD have been employed to find protein structures, ligand prediction and characterization and act as powerful tools for future drug discoveries.

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