

See discussions, stats, and author profiles for this publication at: <https://www.researchgate.net/publication/265599140>

# Exploring the scientific basis of Ayurvedic medicine: A computational approach

Conference Paper · July 1999

---

CITATIONS

0

READS

85

1 author:



Subhash C Basak

University of Minnesota Duluth

558 PUBLICATIONS 11,283 CITATIONS

SEE PROFILE

## aadi katha

### Understanding the Molecular Basis of Ayurvedic Medicine : From Structure-Activity Relationship (SAR) to Composition- Activity Relationship (CAR)

Subhas C. Basak, Ph.D.  
Senior Research Associate  
Natural Resources Research Institute  
and  
Adjunct Associate Professor  
Department of Biochemistry and Molecular Biology  
School of Medicine  
University of Minnesota-Duluth  
5013 Miller Trunk Highway  
Duluth, MN 55811  
USA  
email: sbasak@wyle.nrri.umn.edu

"Darling, you and I know the reason why  
The summer sky is blue,  
And we know why birds in the trees  
Sing melodies too."  
Meredith Wilson, *You and I*

"Ostensibly there is color, ostensibly odor,  
ostensibly bitterness, but actually  
only atoms and the void."  
Galen,  
*in Nature and the Greeks*, by E. Schrodinger,

"Those alone are wise who act after investigation."  
Charaka, **Sutrasthana 10:5**

## *aadi katha*

### A. AYURVEDA IN INDIA AND THE WESTERN COUNTRIES

Ayurveda (ayur=life, veda = knowledge; the science of life or longevity) is the oldest and indigenous medical practice of India. The exact time of origin of this tradition is lost in antiquity. It is estimated that this medical system was discovered in India some time between 500 and 2,000 BC. Some of the most ancient Hindu scriptures like Rigveda and Yajurveda mention various diseases and their remedies (1, 2). About 50-75% of Indians use traditional medicine routinely; the underlying reasons are both a profound faith on the power of traditional drugs as well as a lack of easy access to the western (allopathic) medicine. As of April 1986 there were an estimated 250,000 Ayurvedic practitioners in India as compared to 700,000 doctors of the modern system (2).

Currently, there is a lot of interest in the west about non-allopathic medicine. Collectively, they are called "alternative medicine." Ayurvedic practice, homeopathy, acupuncture, etc. fall under this category. The National Institutes of Health (NIH), the premier funding agency for health science research in the United States, is gradually opening its doors to researchers in alternative medicine in order to broaden the horizon of choices in health care.

### B. AYURVEDIC KNOWLEDGE AND NEW DRUG DISCOVERY

Ayurvedic philosophy characterizes the

constitution of a human being in terms of some fundamental factors. Normal health is looked upon as reflecting a balanced state of the constituent factors (1). Any imbalance of those factors (humors), e.g., **vata**, **pitta**, and **kapha**, will lead to abnormality and disease. Medicinal preparations act by bringing back the balance of these intrinsic factors of the body. More complex methods like diet and **yogic exercise** are also used to restore the balance and cure diseases.

The western (allopathic) medicine is based on the paradigm that a diseased state is produced by abnormalities caused by some extraneous agents (e.g., a bacteria, virus, etc.) or some alterations in the metabolic system. The total constitution of the body is not always the focus of consideration in the mainstream western medicine. The former idea led to the search and successful discovery of various chemotherapeutic agents and antibiotics. Such drugs selectively inhibit the growth and reproduction of the causative organism precipitating the disease. On the other hand, in the case of mental disorders too much or too little concentration of some normal metabolite of neuronal cells might lead to the disease. For example, depression is caused by inadequate availability of biogenic amines at the post synaptic neuronal receptors; the overabundance of amines leads to the opposite psychological state, mania (3). The western system has not been totally oblivious to the role of physiological constitution of the individual in the causation and treatment of diseases. Various warning labels on the bottles of

## aadi katha

pharmaceutical preparations regarding contraindications speak of the sensitivity of the western system to the importance of constitution in determining therapeutic efficacy and potential toxicity. However, constitution is not an integral factor in western medical intervention as it is in the Ayurvedic system. Consequently, the western scientists and drug companies have looked upon the Ayurvedic system of knowledge as the source of new leads for drug discovery. We give below a few examples.

Ayurvedic system uses various plant extracts for treating liver disorders. One such plant is *Aloe Indica*. A major component of *A. Indica*, androgapholide (I, Figure 1) has been shown to prevent the CCl<sub>4</sub>-induced increase of serum glutamic pyruvic transaminase (SGPT) and serum glutamic oxaloacetic transaminase (SGOT) in rats (4). Clinical studies with infected hepatitis patients showed that the plant extract caused improvement in liver function (5).

*Rauwolfia serpentine* (*sarpagandha*, as it is called in India) has been used in Indian traditional medicine for a long time. In the late 1940s and early 1950s, the hypotensive, sedative and antipsychotic properties of the crude extracts were reported by various authors (see Ref. 2 for a review). This led to the discovery of reserpine (II) from *R. serpentina* by

medicinal chemists of the Ciba company in Basel (6,7).

Psoralen (III) was isolated from the seed of *Psoralea corylifolia* (8). This compound promotes the formation of melanin on exposure of skin to UV light. Gum guggul derived from *Commiphora mukul* is an important Ayurvedic drug. Its effectiveness in treating obesity has been mentioned in Sushruta Samhita. Two important hypolipidaemic compounds, (Z)-guggulsterone (IV) and (E)-guggulsterone (V), have been isolated from this gum (2,9).

### C. POSSIBLE APPLICATIONS OF STRUCTURE-ACTIVITY RELATIONSHIPS (SARs) IN AYURVEDIC MEDICINE

Modern scientific research, including biomedical research, is intrinsically reductionistic. This means that the major goal of science is to explain the properties and behaviour of complex entities in terms of the properties of its simpler parts (10). This gives us the mechanistic basis of the observed phenomena and a coherent explanatory power. Modern theoretical physics have succeeded in explaining the vast hierarchy of structures from the tiny atoms to the large scale arrangements of galaxies using a few fundamental forces (11). In the realm of chemical and bimolecular sciences, we

attempt to explain the physicochemical and biological properties of molecules in terms of the properties of constituent submolecular parts. This line of research has led to the development of the science of Structure-Activity Relationships (SAR) the goal of which is to explain and predict the physicochemical, biomedical and toxicological properties of molecules in terms of their structural characteristics. The SAR paradigm can be compactly represented as follows :

$$P = f(S) \dots \text{(Eq}^1\text{.)}$$

where P is any property and Srepresents the appropriate structural descriptors. S can be either calculated molecular descriptors or any experimental physicochemical property like lipophilicity (12-16). SAR techniques have been used primarily in predicting properties of single compounds.

#### i) Characterization of Ayurvedic Drugs from the Properties of Dominant Components

Ayurvedic drugs are usually complex mixtures consisting of hundreds of component chemicals. It is possible that a certain number of molecules in the mixture are responsible for a particular therapeutic activity. One can they try to explain the properties of the whole mixture in terms of the properties of the

components, called **dominant components**, for that specific therapeutic action. If the number of chemicals in the set of dominant components is too large, methods of molecular similarity/dissimilarity can be used to cluster them into groups of analogous compounds. In the most ideal situation, chemicals which are similar by some appropriate measure should have similar biological activity. Such research could be called **Composition-Activity Relationship (CAR)** instead of the traditional SAR.

How do we do the clustering? One possibility is to use experimental data determined for the chemicals. However, in many instances of real world chemistry the majority of the chemicals will have no or very little experimental data. In that case similarity methods based on theoretically calculated molecular descriptors can be used for clustering. Our laboratory has been involved in the development and use of non empirically based similarity methods (17-19).

#### D. TOXICITY ESTIMATION OF AYURVEDIC DRUGS FROM SARs

Every chemical substance has some potential toxicity. Some chemicals with specific structural characteristics (pharmacophoric or toxicophoric pattern) have high toxicity; others with no such

## *aadi katha*

specific structural attributes have nonspecific toxicity. Even naturally occurring compounds can be very toxic. It would be advisable if one could estimate the potential toxicity of the dominant components of the Ayurvedic drugs before their use. One way to do that is to test them in the laboratory. However, the resources for toxicological testing are very limited. The other alternative is to use computational methods for predicting potential toxicity of chemicals from their structure. Our research group at the Natural Resources Research Institute has been at the forefront of the development of computational methods for predictive toxicology (20-24). Such methods can be used in toxicity estimation when experimental data for hazard assessment are unavailable.

### E. CONCLUSION

About 33% of Indian doctors come from traditional medicine. A large fraction of the Indian population uses traditional medicine, including Ayurvedic drugs, regularly. SAR methods can be useful not only in predicting potential therapeutic activity of the dominant components of Ayurvedic preparations, but also in assessing the potential toxicity of the constituents of such therapeutic agents. Such SAR studies can illuminate the role of various structural features in determining their therapeutic efficacy. For complex

Ayurvedic drugs, clustering and molecular similarity methods can be useful in their classification and molecular characterization.

### F. ACKNOWLEDGEMENTS

This article is contribution number 166 from the Center for Water and the Environment of the Natural Resources Research Institute, University of Minnesota, Duluth. This work was supported, in part, by grant F49620-94-0401 from the United States Air Force.

### G. REFERENCES

1. Verma, V., **AYURVEDA : a way of life**, Samuel Weiser, Inc., York Beach, Maine, USA (1995).
2. Anand, N., Contributions of Ayurvedic Medicine to Medicinal Chemistry, In : **Comprehensive Medicinal Chemistry**, Hansch, C. (Ed.), Vol. 1. pp.113-131, Pergamon Press, New York (1990).
3. Baldessarini, R.J., Drugs in the Treatment of Psychiatric Disorders, In : **The Pharmacological Basis of Therapeutics**, Gilman, A.G., Rall, T.W., Nies, A. and Taylor, P. (Eds.), pp. 383-435, Pergamon Press New York (1990).
4. Chowdhury, B.R. and Poddar, M.K., IRCS Med. Sci., **12** 466 (1984).
5. Singh, K.P., J. Int. Inst. Ayurveda, **2**, 208 (1983)

6. Muller, J.M., Schittler, E. and Bein, H.J., *Experientia*, **8**, 338 (1952).
7. Dorfman, L., et al, *Helv. Chim. Acta*, **37**, 59 (1954).
8. Jois, H.S., Manjunath, B.L. and Venkataraman, S., *J. Indian. Chem. Soc.* **10**, 41 (1933).
9. Dev, S., *Proc. Indian Acad., Sci., A*, **54A**, 12 (1988).
10. Weinberg, S., *Dreams of a Final Theory*, Vintage Books, New York (1993).
11. Davies, P., *The Accidental Universe*, Cambridge University Press (1993).
12. QSAR : Quantitative Structure-Activity Relationships in Drug Design, Fauchere, J.L. (Ed.), Alan R. Liss, Inc., New York (1989).
13. Basak, S.C., *Med. Sci. Res.*, **15**, 605 (1987).
14. Basak, S.C., Niemi, G.J. and Veith, G.D., Recent Developments in the Characterization of Chemical Structure using Graph-Theoretic Indices, In : **COMPUTATIONAL CHEMICAL GRAPH THEORY**, In : Rouvray, D.H. (Ed.), pp.235-277, NOVA, New York (1990).
15. Basak, S.C., A Nonempirical Approach to Predicting Molecular Properties using Graph-Theoretic Invariants, In : **PRACTICAL APPLICATIONS OF QUANTITATIVE STRUCTURE-ACTIVITY RELATIONSHIPS (QSAR)** IN ENVIRONMENTAL CHEMISTRY AND TOXICOLOGY, In : Karcher, W. and Devillers, J. (Eds.), pp. 83-103, Kluwer Academic Publishers, Dordrecht/Boston/London (1990).
16. Basak, S.C., Gurnwald, G.D. and Niemi, G.J., Use of graph theoretical and geometrical molecular descriptors in structure-activity relationships, In : **FROM CHEMICAL TOPOLOGY TO THREE DIMENSIONAL MOLECULAR GEOMETRY**, Balaban, A.T. (Ed.), pp. 73-116, Plenum Press, New York (1997).
17. Basak, S.C., Gute, B.D. and Grunwald, G.D., *J. Math. Chem.*, submitted (1997).
18. Basak, S.C. et al, *Discrete Appl. Math.*, **19**, 17 (1988).
19. Basak, S.C., Bertelsen, S. and Grunwald, G.D., *J. Chem. Inf. Comput. Sci.*, **34**, 270 (1994).
20. Basak, S.C., Niemi, G.J. and Veith, G.D., *J. Math. Chem.*, **4** 185 (1990).
21. Basak, S.C., Niemi, G.J. and Veith, G.D., Mathematical and Computer Modelling, **14**, 511 (1990).
22. Basak, S.C. and Grunwald, G.D., SAR and QSAR in Environmental Research, **2**, 289 (1994).
23. Basak, S.C. and Grunwald, G.D., *J. Chem. Inf. Comput. Sci.*, **35**, 366 (1995).
24. Basak, S.C. and Grunwald, G.D., *Chemosphere*, **31**, 2529 (1995).

