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PHCOG MAG.: Discussion (New Section)

Research on Herbal products/extracts: Where does it stand?

Discussion initiated by Dr. Shoheb Qureshi

Most of the top ranking international journals of the world have almost common remarks about the work on crude herbal products. I have written their remarks hereunder and would like to share their opinion with the members of Phcog. Although, the study on active agents cannot be dispensed with, the work on herbal products/extracts is also very important. The two are difficult to go together due to the exorbitant size of work. Nevertheless, in matter of harm, the significance of isolated constituents would not be different from the synthetic drugs. Here, I wonder, if there is anything wrong to work on the herbal products (the form they are available for human consumption) and support our results with the available literature on the active constituents. Under the circumstances and priorities, there are ample scopes for many international journals coming up to cater the publication needs of the natural herbal drugs in the form they are available for human consumption. Remarks of some of the top most international journals on work related with herbal products:

Studies involving natural products (crude extracts) are unlikely to be accepted. All the authors are encouraged to transition to studies conducted with purified agents as soon as possible. All active agents must be adequately characterized and identified, especially when an extract is used as a convenient source of an active agent. Identification should include chemical name (CAS registry number, EU number, etc), as well as common name where appropriate and the source of the chemical or agent studied.

Dr. Shoeb Qureshi

I too agree that there is lot of thirst to work with the isolated constituents from herbal extract. Please clarify me in this regard. One of the beauty with herbal extract is its multicomponent, many times it pave the way to beneficial effects and nullify fewer side effects also (of course it is generalized concept, there are exceptions too).We may not experience the same with the isolated constituents.

Suba

Actually isolated compounds are having their specific activity; one should check first what compound are isolating, see whether it is in pure form then check its activities. Though plant may have various activities single compound may be responsible for some or other activity.

Radhika.

Yes, what Radhika says "Though the plant may have various activities, single compound may be responsible for some or other activity" is correct. However, the same single compound could be toxic like some synthetic formulations. Although, the protective constituent/(s) in the natural drugs could bring up a defense, the lacuna is that some component/(s) in the same cocktail may influence cytochromes to jeopardize the metabolism. It could be a welcome-relief, if the inhibition restricts break-down of the component/(s) with deteriorating effects; but it can also be the other-way-round and the beneficial constituent/(s) might become the escape-goat. Thus a lot of theoretical studies on structure activity relationship of the beneficial and toxic moieties of the known compound/(s) would be a boon for the discovery of some novel drugs from plants.

Dr. Shoeb Qureshi

With due regards to member opinions, I would like to share a parallel but emerging trend in botanical drug research. I understand good impact journals do not accept papers if extract is not chemically characterized. Even I have gone through the same problem there and then. But with the emergence of system approaches in drug discovery this scenario is likely to be changed. I request you all to go through the recent issues in Drug Discovery Today journal where the drug discovery community is now focusing on a shift from single gene-single target-single molecule to multiple gene-multiple target-multiligand approaches in drug discovery. With this approach, the importance of complex mixtures like botanicals is going to increase. As they may act as source for discovery of synergistic moieties acting simultaneously or concurrently on multiple targets and restoring homeostasis. Recently my review focusing the importance of botanicals in such drug discoveries got published in Drug Discovery Today. This is first time that they accepted such a review. I will be happy to share with you all. But this does not imply, that there will no need of dereplication of extracts. As a scientist working in herbal research I strongly feel that we all must strive and develop newer approaches for ensuring quality and reproducibility in these novels biological mixtures.

As a member of this group, I strongly feel that let us all get together and prepare a master manuscript highlighting importance of complex mixtures over mono-substance agents and send it across to all high impact journals editors and get there views and finally publish it in a high impact journal. This will be a good contribution from all of us towards highlighting the importance of herbals. This will be a combined publication of all interested PHCOG members. I will be

waiting for your views on that. I will request even editors of PHCOG to give their opinion on this. Kindly do send me your views, what do you all think about this.

Manish Gautam

With all due respect, you have lost more than half your audience because they will have given up on the 'techno-babble - speak" of your post. For clarification, are you saying that multiple actives (which often occur naturally in vegetable drugs) are the way forward for synthetic pharmaceutical actives?

Kendra

The entire problem with synthetic pharmaceuticals is their toxicity. Today the world want a change in the therapeutic approaches. The concept of "multiple actives for synthetic pharmaceutical actives", according to earlier correspondence in the series, would really be a welcome relief for the synthetic pharmaceuticals. The development of synthetic drugs with these thoughts would definitely avert the negativities of these drugs, such as adverse effects, drug resistance, interactions, mutagenicity and carcinogenicity of the anti-cancer drugs, drugs disrupting the hormonal balance and many more…….. The development of antioxidant-oriented synthetic drugs would fight toxicity to some extent. Like wise, the drug resistance, drug interactions and other adverse effects can be taken care by specific designs in the multiple actives. Ofcourse, researches must be taking care to fight against the intricacies! Like wise, there are active pharmacognostic approaches to potentiate therapeutic efficacy in fractionations with continuos eradication of less effective and toxic fractions. The progress is ongoing and the results will be glorious !!!! Nevertheless, steps ahead with the isolations would eliminate the disagrements and controversies between the natural and the unnatural ! Is it like this ?

Dr. Shoeb Qureshi

Thanks Dr. Quershi for clarifying my view. I am attaching herwith a article highlighing importance of botanicals in future discoveries. I hope this will make my view more clearer. I am still waiting opinions from other members. Kindly find the article.

Manish Gautam

I very much like the Dr. Gautam's idea of putting together a manuscript on chemical mixtures in pharmacotherapy. Almost 10 years ago (December 1996) David Ho was awarded the "Man of the Year" award by Time Magazine (a popular publication in the US) for developing the anti-HIV cocktail. Enough time has passed since then, conventional wisdom is clearly going in the direction of multiple targets and multiple ligands, particularly to combat infectious diseases. To have the manuscript on the phcog.net website by 2006 would be neat, as that will be the 10th anniversary of synergy going "mainstream". It would be great if the manuscript would also serve as a manual to guide investigators who wish to study pharmacological properties of phytomedicines. This is very complicated. If activity is lost in the course of in-vitro bioassay-guided fractionation of a crude active extract, does it mean chemical degradation has occurred, or does it mean synergistic compounds were separated? If the latter, how to proceed? For the time being I would argue that once activity is lost we should note it, perhaps repeat the experiments, report the findings, and go on to the next lead. We presently don't know enough about biology to waste our precious time chasing "synergy" in cases of lost activity. There are maybe 30,000 "genes" in our chromosomes and we know of maybe 500 [approved] drug targets (i.e. doctors know how to affect less than 2% of our genes). In that sense, we know almost nothing about ourselves. The best we can do to unravel synergistic interactions at present is to isolate multiple compounds from active fractions, test them together and individually, and see if the math indicates synergy, addition, or antagonism. I continue to find it remarkable that PhDs spend time writing papers about the pros and cons of natural products and ruminating on whether or not there is any reason to study them, when they could be discovering new targets and ligands! There are only maybe 10000 plants that have been used in traditional medicine and only a few 1000 used routinely. How valuable would it be to test all of these plants against all the known drug targets? Would it be even worth doing at this point since we know so few targets? This is such an exciting time for drug/target discovery and clearly traditional medicines have much left to offer. However, people sometimes jump into this too fast and carry out studies on uncharacterized or poorly characterized plant material. A web-based "handbook" for carrying out MULTIDISCIPLINARY Pharmacognosy research aimed mainly at biologists/pharmacologists/MDs would be a welcome addition to the phcog.net website!!

Luke Chadwick

Multiple actives seem to be an interesting concept. I doubt if in many areas it would be cost effective. For example herbal anti-malarials from Artemisia annua contain very many actives - possibly more than twenty so far identified, but new synthetics based around synthetic modifications of just one of the principle actives continue to be developed and marketed (see www.cropwatch.org - papers on malaria & mosquitoes etc). This gives a brief period of respite for any in the exposed population which can afford the drugs, but drug resistance invariably develops after a few years, during which time the pharmaceutical companies have made their money from the new synthetic. We are told in the promotional hype surrounding these products that the development of more effective and long-lasting natural herbal preparations would be too expensive. I don't believe this, and it is all too easy to cynically believe that pharmaceutical industry has

no wish to eradicate disease, but only to make profit from suffering.

Toxicity is an area where some corporate have been playing a very dirty game - the scandals of the last year need no further mention. But part of this unfairness is to point fingers at the toxicity of herbal medicines and confuse "expert" committees by forwarding selective information on toxicity which puts naturals in a bad light. This means that poorly financed scientists who work in the alternative medicine area (and who are not on corporate expenses) have to spend their own time and money defending these slurs against perfectly good products.

Kendra.

I wholly agree to you on this. We all are sensitized to these issues but we do little to highlight these issues in proper perspective. PHCOG has brought natural product scientists to a common platform. My only request is let us get together and do something to bring these issues to a proper perspective. PHCOG being an international and interdisciplinary group has the right content to complete this endeavor.

Manish

Thanks for your message and i appreciate your views about the present discussion going on from past one week, Its really amazing to know the coincidence and idea of Dr. Chadwick, As i was about to propose or give a call on such web based book "An Open Access to All researchers" titled "COMPREHENSIVE RESEARCH IN PHARMACOGNOSY".

I promise, on behalf of Phcog.net to encourage this idea and make it reality. As one of the Board of Directors, i will put forward this active discussion in next meeting of Phcog.net. Phcog.Net comprises 682 members in just one year. I hope, if each one of us contribute atleast a single piece and genuine information, it will be a great contribution to the field of pharmacognosy. Further, The discussion will also be included in next issue of Phcog Mag. as a new column, PHCOG MAG: Discussions.

Mueen Ahmed K K

I thank you for the effort of publishing the discussions in the phcog mag issue. The discussion seems to be heading towards to a very good direction. I would be happier, if all of us can get together on a common platform and prove the usefulness of the multiple targets and synergism to the modern world. If this discussions or atleast the summary appears in the phcog magazine, it will be great reading. I thank Dr. Mueen Ahmed for the same. Sir, also please wait for some more members to participate in the discussion before publishing the same.

M. Vijayakumar

Joining the ongoing discussion on the synergism and multiple targets. I have a point. We cannot deny the fact that the so called modern medicine or the synthetic medicines (allopathic) has achieved the pinnacle and is the catering to almost all the diseases through out the world. It is so dominant that the other systems of medicine have become "ALTERNATE MEDICINE" or "Complimentary medicine". But actually it isn't. Especially in countries like India, where Ayurveda was the original medicine and this modern medicine came much later. Then we need to understand why this modern medicine became the main medicine and Ayurveda became the alternate medicine in the due course of time.

The undeniable fact is that the in the case of the allopathic medicine, every fact is known and transparent. It (label) says it causes this toxicity. They accept the fact. The mechanism of action (for most drugs) is also known.

We realize that plant drugs or extracts have synergism. But we need to prove it through proper pharmacological studies and also the multiple targets that they act upon have to be shown. Because as a researcher we are happy, but as a consumer, he has to know the details. That is precisely the reason i think where we have lacked and modern or synthetic medicines have taken over. That is why people still take modern medicine.

So, i believe that we all should make a concerted to show the synergism on paper through proper pharmacological The mere statement that herbal drugs are safe and less toxic, is no more good. This also has to be proven with data. We all know it is true, but it is time to show to the world. It actually is true. So, let us make an effort to go back to the lab and prove synergism.

R Govindarajan

I would like to express my views too. People are also confused regarding availability of Pure herbal drugs, they don't believe that what powder they get is authentic. Awareness regarding herbal drugs should be created among common public. Since big names of companies are not labeled for herbal drugs people don't believe in it. We need to change this trend. For that instead of just doing research for herbal drugs first catch the market for them then do alterations. You tell me How many people who have published their research papers have actually worked out for market values of their search?. I feel none. Just doing PhD or Publishing thousands of paper has become target of today's generation who are doing their job as Pharmacognosist.

Radhika.

Thanks for supporting my idea. My special thanks to Dr Chadwick for suggesting the manuscript at David Ho anniversary. This will be an excellent idea and will be a true tribute to a great scientist. I also thank and appreciate the prompt encouragement and initiative taken by Dr. Ahmed. Let's wait for other members comments and then will work on the rough outline of the manuscript.

Manish

I am accepting manish view for finalizing the manuscript. We will wait some more time to get other viewers opinion. I am surprising the members discussion

over the week and that one is encourageable one among the pharmacognosist.

D.Ashokkumar

I would like to add one more point on this discussion. When a same herb is collected from various region atleast few of them show differences in their chemical make up. I believe we also have to address this issue properly.

Suba

The points raised by you are worth mentioning and needs careful consideration by the members of PHCOG. It is a fact that there is utter confusion and chaos in sales and availability of herbal medicines for human consumption. Leave alone the purity of these drugs, there is nothing systematic and there prevails a "law of jungle". Most of the plant medicines available in the market have no mention for (i) the dates of manufacture and expiry (ii) botanical name and contents (iii) prescription leaflet including the therapeutic values, interactions, toxicities. However, some companies are shrewd enough to give attractive trade names. Sometimes, evil minded businessmen dare to adulterate the valuable herbal products with allopathic drugs. Thus, the presentation of these medicines is quite awkward and very dubious. This is all because there is no quality control on these medicines. Through out the world, these medicines are considered to be dietary supplements and hence skip the rigid measures of controlling the quality. Infact there should be thorough evaluation for chemical constituents, pharmacology, toxicology, pathophysiology, microbiology, and ..... of these medicines before they are available for human consumption. Here, I would like to say that this is the concern of the respective ministries and the Governments to impose rigid quality control measures on herbal drugs, just as it is done for synthetic drugs. Scientists, researchers, teachers and students of this discipline have no control on the markets. They are just like a helpless common man. But as we are scientifically literate, it is our job to protect the valuable products from greedy businessmen and quacks. We can make campaign through media and our writings to impress upon the government to regulate quality control measures on the herbal drugs on par with the synthetic drugs. It is then, when the subject can get prominence and the values will be recognized by the companies selling the herbal products.

Dr. Shoeb Qureshi

I fully agree with your statement that it is important to educate the massess. I also agree that researchers are more in publishing and not in to market research. But kindly tell me, how you are going to go to the masses, without results of performance. Today's public is more aware. They have various sources of information. Many people have access to wide source of information and they want data. They are more aware of the terminologies now. You just cannot say to them, since it is herbal, it is safe and even i don't agree with the big companies. It is a factor to an extent, but unless the product is good, it will not sustain. So we researchers should make an effort generate data to instill confidence in the minds of people. The statement "Anything herbal is safe" does not hold anymore. Today's common man wants to have toxicity data. He realizes that anything and everything is not safe. He drinks mineral water even at home. Such is the development of science. I am not trying to say that herbal drugs are not good. It is good and is in time tested since many years and ages. But, it is our turn to provide scientific base and prove it really is worth it.

R Govindarajan

LAME EXCUSES THAT SUPPORT A DISCUSSION ON HERBAL MEDICINE

In recent past, the discussions of PHCOG have become very interesting. This has lead many of our learned friends to come forward and give their valuable suggestions. With this impression in mind, I would like the members to discuss the pros and cons and the lame excuses that generally support weak points in our results and in matter of comparisons with other data. Here are six points that often supports and/or hinder the delicacies of results and discussion of a herbal drug.

(1) Differences in the content of constituents in samples drawn from different geographical locations.

(2) Different fractions of a same plant having different activities.

(3) Difference in extracts and variations in the constituents of the same plant

(4) Different parts of the same plant having difference in the constituents and activity.

(5) Seasonal variations and the difference in the constituents of plants.

(6) Unstable oxidants/antioxidant constituents in plants.

In this regard I would like our friends to discuss (i) if it is possible to exclude these lame excuses from our discussions? (ii) How the plant medicines can be given a uniform pattern around the globe? (iii) How best the green houses would be feasible to eliminate the differences? (iv) Can these green laboratories be maintained on universal standards through out the world?

DR. SHOEB QURESHI