For thousands of years, ingredients from Ayurvedic medicine (though often not in controlled clinical settings) have been connected to efficacy in man—point in case, the introduction of the antihypertensive drug reserpine derived from Rauwolfia serpentina Benth. Additionally, natural products present in Ayurvedic formulations form an interesting source of new molecular entities. This is particularly compelling since from 1981 to 2007, 67% of the new medicines introduced in the “western” world could be traced back to natural products themselves, or they were natural product-inspired. Furthermore, Ayurveda relies on the synergies of the different ingredients in a formulation, to not only cure the disease in question but also reduce side effects and improve adaptive resistance. This approach is now also more and more considered in other cultures, such as by considering combination treatments of drugs.

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Website: www.jaim.in

DOI: 10.4103/0975-9476.113882
acceptance of Ayurvedic approaches. Four of these challenges were recently outlined by Corson and Crews: (i) the isolation of active constituents; (ii) the synthesis of active constituents; (iii) the elucidation of the mechanism of action (MOA); and (iv) the development as a drug. In particular, the elucidation or explanation of the MOA is of relevance to our current work that has recently been published and which we would like to alert you to with this article, in order to offer one possibility of bridging disease and treatment perceptions of both traditional and “western” schools of thinking. Given the renewed interest in the west into traditional approaches to healing, our work has also found considerable resonance in western news media, such as with the BBC.

In our study, we employed the use of computational (“in silico”) methods to predict protein targets modulated by compounds used in Ayurveda, as well as traditional Chinese medicine, and subsequently aimed to understand the MOA predictions of active ingredients in the context of their therapeutic uses. While further details and successful examples are given in the publication, we will only illustrate our abilities to rationalize MOAs for Ayurvedic medicines here, analyzing a set of active ingredients from the Indian Plant Anticancer Compounds Database as shown in Table 1. (Interestingly, both in the “west” and in the realm of traditional medicines electronic databases have recently developed greatly; the equivalent database in the context of “western” drug discovery is the ChEMBL database which we also employed in the study described here.) The first compound, labeled as CHEMBL273862 (10-hydroxycamptothecin), is a derivative of the anticancer compound camptothecin of the Camptotheca acuminate plant and the second compound, labeled as CHEMBL463810 (Cholesta-4,25-diene-3,6,24-trione) originated from the red alga galaxaura marginata. As outlined in Table 1, we can show that the targets predicted for the two compounds are consistent with the information in the literature to be involved in cancer pathogenesis, and hence, we anticipate that linking ayurvedic and “western” understanding of disease and treatments is a very fruitful option to pursue in the future.

### Table 1: The target(s) predicted for two active ingredients of Ayurvedic medicines used against cancer, as annotated in the Indian Plant Anticancer Compounds Database.

<table>
<thead>
<tr>
<th>Structure</th>
<th>Predicted target(s)/annotated target in ChEMBL</th>
<th>Literature support</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHEMBL273862</td>
<td>DNA topoisomerase 1 ER-β</td>
<td>DNA topoisomerase facilitates the separation of the DNA strand for the purpose of replication and transcription. Camptothecin, an anticancer drug discovered from the Chinese tree, Camptotheca acuminate blocks this enzyme. ER-β was found to be expressed in breast cancer with ER-α and PR.</td>
</tr>
<tr>
<td>CHEMBL463810</td>
<td>Steroid 5α-reductase 1 Steroid 5α-reductase 2</td>
<td>Both enzymes have been found to be involved in the progression of prostate cancer. The concentration of steroid 5α-reductase 1 have been found to be higher in malignant prostate cancer, whereas steroid 5α-reductase 2 was more pronounced in the benign state.</td>
</tr>
</tbody>
</table>

ER-β=Estrogen receptor-β, PR=Progesterone receptor.
approaches from traditional medicines, such as Ayurveda, with “western” understanding of chemistry, targets and pathways, is a very fruitful avenue to understand in more detail how traditional medicines work. Admittedly, this will be difficult to achieve in many cases, since active ingredients are often not known, and the same can be said for bioactivities of chemical structures as well as our scarce knowledge of the impact of modulating protein targets on disease states. Still, given that Ayurveda starts with the ability to modulate a disease-relevant phenotype (which has been frequently a reason for concern in “western” medicine\(^{[44]}\) combined with our growing knowledge in databases of the above types, we anticipate that methods such as the one presented here will increase in importance in the future. We hope that this development will be mutually beneficial; to learn on the one hand more about the inner workings of traditional medicines, and on the other hand to eventually also increase recognition of traditional ways of treating disease in the “western” world.

Finally, we would like to leave the readers with a few suggestions to advance the case of Ayurvedic medicine, particularly but not only in the “western” world:

1. Utilizing and integrating novel analytical methods, in particular given the advancements of “omic” technologies, that enable the simultaneous study of multiple molecular effects of Ayurvedic treatments using, for example, metabolomics, genomic, as well as proteomic analysis, and

2. Sharing information about experimental data and clinical results from Ayurvedic studies with the public in an easily accessible way. In the opinion of the authors, many of the assumptions being made about Ayurvedic medicine “in the west” are simply based on lack of reliable and accessible information.

ACKNOWLEDGMENT

The authors thank Universiti Teknologi MARA, Malaysia, Ministry of Higher Education of Malaysia and Unilever for funding.

REFERENCES


Source of Support: Nil, Conflict of Interest: None declared.