Rethinking conventional approaches to the detection, management and amelioration of disease

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The linear-leaved water primrose (*Ludwigia hyssopifolia*), with its distinctive yellow flowers and matted undergrowth, is easily recognized along paddy fields and tropical wetlands especially in South and South-East Asia. Also known as the seedbox because of its distinctive dimorphic seeds, it has the potential of being an invasive pest and is classed ‘serious’ or ‘principal’ weed in many countries. It is used locally for composting and in the concoction of traditional remedies in an unscientific and informal manner. In common with other plants of the willow herb or evening primrose family, this weed could turn out to have immense and economically viable pharmaceutical potential. Das *et al*¹ have reported moderate anti-tumor and antibacterial activities in extracts and in an alkaloid piperine from *L. hyssopifolia* and Mohammad *et al*² demonstrated anti-diarrheal properties in a methanol extract. It is noteworthy along the same line that the work by Luximon-Ramma, *et al*³ on Mauritian exotic fruits strongly advocated the use of the red and yellow *Psidium cattleianum* Sabine ‘Chinese guava’, in nutritional programs due to their exceptionally high antioxidant potencies attributed to their rich vitamin C and phytophenolic profiles. These plants are also generally considered as invasive causing havoc amidst the protected endemics of the island and using an ecological conservation approach, indeed legitimate, to safeguard threatened plants from extinction, the systematic removal of Chinese guava trees may deprive us of important sources of active nutritional biofactors.

In a study that features in this issue of the Archives of Medical and Biomedical Research, scientists at the University of Dhaka have further formalized the pharmacotherapeutic potential that this much-derided weed may hold. They studied the effects of hexane, ethyl acetate and methanol extracts of whole plant parts of *Ludwigia hyssopifolia* on carrageenan-induced paw edema, acetic acid-induced writhing, and diuresis in mice. The hexane extract and ethyl acetate extract showed significant inhibition of experimental paw edema. All three fractions significantly inhibited writhing and, in comparison to furosemide, exhibited good diuretic activity.
This study emphasizes the need to look back at traditional healing systems as well in the search for hitherto unidentified molecules with pharmacological activity that may have been tried and tested for generations, but are now in danger of being forgotten. It is regrettable, yet a sign of our times, that patent issues and proprietary controversies as well as economic considerations are greater drivers of pharmacologic research than the pattern of human disease and suffering.

On a similar note, the need for cost effective drugs is higher in the developing world and this is perversely offset by the lowered purchasing power of the masses. It behooves local pharmaceutical firms to make available to the health services indigenous customizations of drugs and dosage forms that combine economy and availability without compromising quality and efficacy. Given the vast demand for proton pump inhibitors among Bangladeshi patients and the economic climate that shapes availability and demand, a cheap yet efficacious formulation of omeprazole would fit the bill. Losec® MUPS®, omeprazole magnesium in a patented Multiple Unit Pellet System, would appear to be the reference standard against which alternatives would have to be measured.

An open-label, randomized, two-treatment, two-sequence, two-way crossover, single-dose bioavailability study carried out on Bangladeshi volunteers established the bioequivalence of Proceptin, a locally manufactured capsule form of omeprazole by showing no statistically significant differences in plasma concentration-based bio-availability parameters. The study, detailed in this issue, also noted pharmacokinetic patterns characteristic to the Bengali population under study. Given the worldwide trend towards lowering restrictions on omeprazole, this study has greater implications that extend beyond the research laboratory into the world of corporate pharmacy and across the minefield between intellectual property rights and universal human beneficence.

In another research work published in this issue, the authors sought to assess the sero-prevalence of rubella-specific IgM antibodies in pregnant women in Zaria, Nigeria. Rubella, or German measles, is a viral contagion that causes a transient morbilliform rash, low fever and lymphadenopathy. In contrast to its benign course in children and young adults, an affected pregnant woman suffers Congenital Rubella Syndrome whereby her fetus is transplacentally affected and may suffer birth defects, stillbirth or miscarriage. The study found an unusually high prevalence of near 40%, which takes on added significance when one recalls that raised IgM levels last only a few weeks after infection before dropping back to baseline levels. This high sero-prevalence has never been reported in previous literature and can only be explained by postulating the occurrence of an outbreak during or just preceding the study period. This goes to show the frequency and prevalence of rubella in the population and how outbreaks of sub-epidemic proportions can go unrecognized, all of which underline the great risk the pregnant woman and her unborn fetus face. Even women who knew about rubella were affected, thus showing that education was no protection because of the high endemicity of the infection. More than anything else, the research outcome emphasizes the dire and pressing need for a national rubella vaccination program in Nigeria and, by extension where relevant, in the developing world.

The inexorable battle against the diabetes epidemic that faces us is marked by progress in all spheres and, just as any winning army faces the additional burden of wounded survivors, healthcare resources and facilities worldwide are increasingly having to deal with chronic and advanced
complications that, in a bygone era, would have proved fatal at a much earlier stage. Perhaps it is a measure of our diagnostic and therapeutic progress that, apace with the growing quantum, the spectrum of diabetic complications being encountered is both widening and shifting towards the dire end of severity and chronicity. Since the success of most diabetic interventions depends upon a rigorous degree of regimentation (and motivation) in matters of diet, lifestyle and medication, it is revealing to look at the interplay of cognitive function, especially in the growing population of elderly diabetics, on matters of health self-efficacy and compliance. An opinion paper in this issue analyses the complex inter-dependency of these factors and makes a strong case for a battery of simple tests that can routinely screen for mild cognitive impairment in the vulnerable groups, and thus customize treatment regimens for not only optimizing compliance but also to slow the progress of dementia. The authors expound on the incidence of diabetes-related cognitive deficiency in emerging countries with aged population like India and China posing inevitably potential management problems of our elderly in countries where life expectancies are on the rise. This opinion paper is in congruence with the recent study from a Johns Hopkins University group5, which strongly determined through a cohort study that diabetes prevention, and glucose control in midlife may protect against late-life cognitive decline. In addition to medication, lifestyle and diet compliances this paper emphasizes the importance of a further tenet, “Health Self Efficacy” that would complement efficiently the fight against cognitive decline.

Non-compliance to interventions for diabetes also relates to their innate unpleasantness. Green tea however has the refreshing and unusual attribute of being a scientifically validated positive intervention for diabetics that may be considered pleasant and palatable, almost an indulgence. Various experimental animal models have conclusively shown the salutary efficacy of green tea. In a short communication to this journal, this has been taken further by a study that assesses the effect of green tea on a renal cell line in an oxidative stress-induced diabetic milieu. This study was designed to evaluate energy metabolism in human embryonic kidney (HEK-293) cells stimulated with various concentrations of hydrogen peroxide, and showed that green tea extracts promoted their viability and protected against oxidative stress-induced mortality. This could be attributed to the free radical scavenging propensity of the green tea catechins and suggests that dietary supplementation of green tea as a beverage could be renoprotective in diabetic patients, delaying the onset and progression of diabetic nephropathy.

In an opinion piece that rounds off this issue, the authors look at the role of Memantine and one-on-one caregiver contact in reducing the dose of anti-psychotic medication in the management of dementia. Whether consequent to Alzheimer’s disease or of vascular etiology, dementia causes cognitive decline and behavioral and neuropsychiatric changes that ultimately require the use of medication that in itself increases morbidity in the form of infections and cardiovascular incidents.

An option with potential to reduce the dosage quantum would be to combine cognition enhancers (cholinesterase inhibitors such as donepezil, galantamine and rivastigmine) with Memantine, a non-competitive antagonist of the N-methyl-D-aspartate (NMDA) receptor, that provides a degree of neuro-protection. This could be further improved by one-on-one caregiver contact including the adoption of
psychosocial interventions such as redirection and multisensory stimulation. There is need, the authors opine, to explore these research avenues, as dementia is an ever-increasing public health concern. It affects a vulnerable veteran population incurring a large caregiver burden and significant financial expenses. Any intervention that has the potential for cognitive or behavioral improvement in the social function and self-care of these patients, without a commensurate increase in side-effect morbidity, is to be actively sought and pursued.

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REFERENCES