that encoded proteins not known to be related to the mode of action of the drug. Thus potential new drug targets in isoniazid sensitive and resistant strains could be identified. Therefore one objective may be considered the removal of 'bottle necks' in the process of target identification [4, 5].

Structural genomics

As noted in a recent review in *Science* [6], structural biology has turned the corner. We are seeing today that modelling and high speed computing is allowing greater accuracy in the processes of predicting protein structure.

This approach has limitations, a classic example being the impact of molecular chaperones on the final conformation of a protein. However, it is not unreasonable to expect that advances in this field will facilitate the development of better computational systems.

We are approaching a time when biomedical science will have the tools that will allow both the identification of novel therapeutic targets and allow us to model drug-target interactions. That is, identify targets and design novel lead compounds *in silico*. Indeed, we may even be able to test for potential adverse effects and/or selective toxicity using the same technology.

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Old therapies, new science

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With the emergence of antibiotic resistance as a major public health problem and the apparent decline in pharmaceutical company drive to produce new antimicrobials, there has been an increase in interest in revisiting remedies and agents once popular before the advent of the antibiotic era [1].

This makes sense – it is obvious that many of these therapies worked hundreds if not thousands of years ago, although the scientific basis of some is rather obscure. With others, however, good data exist on both *in vitro* and *in vivo* efficacy. Randomised clinical trials have been completed with good outcomes. Three compounds or groups of compounds used in traditional medicine – in which there has been a major resurgence of interest in the last 30 years to the extent that one has become an accepted therapy – are garlic, artesunate and essential oils.

Garlic

Garlic *(Allium sativum)* was once used by millions to ward off vampires and was first prescribed in 3000 BC by the Sumerians, a group who lived and still live in present day Iraq. Garlic has a wide spectrum of action and is considered to be antibacterial, antiviral, antifungal and antiprotozoal [2].

However, although garlic has been used for its medicinal properties for thousands of years, investigations into its mode of action have only occurred relatively recently. Early steps in identifying the active constituents of garlic were the discovery that the compound allicin (allyl 2-propene thiosulphinate) is formed when garlic is crushed and that its formation depends on the action of the enzyme allinase.

Methyl and allyl sulphide derivatives of allicin are formed by the steam distillation of crushed garlic [3]. The diallyl sulphide components of garlic oil are the most active and this activity is inversely proportional to the number of disulphide bonds, diallyl monosulphide having greatest activity. These diallyl sulphides inhibit various bacteria and fungi at concentrations similar to conventional antimicrobials [4].

Several recent studies have shown good activity of garlic materials against *Helicobacter pylori* [5] and clearly garlic has a long history of safe use. Epidemiological studies show a reciprocal relationship between gastric cancer, which is strongly correlated with *H. pylori* infection, and the consumption of *Allium* vegetables [6], suggesting the further investigation of garlic as an antimicrobial is warranted.

Artesunate

Traditional Chinese medicine has provided us with qinghaosu for the treatment of malaria. The isolation of artemisinin in 1972 by a Chinese scientist lead to the development of a number of derivatives and an impressive body of work relating to the understanding of the chemistry, pharmacological profiles, toxicology, metabolism and effects on the malaria parasite [7].

One area where progress has been slow is determining a mechanism of action. A randomised trial of the combination of artesunate followed by mefloquine was highly effective and well tolerated in patients with acute uncomplicated falciparum malaria in Thailand [8].

Essential oils

The antimicrobial activity of plant essential oils and extracts has formed the basis of many applications, including raw and processed food preservation, pharmaceuticals, alternative medicines and natural therapies [9]. Only a few of the oils used on the basis of their reputed antimicrobial properties have well documented *in vitro* activity and even fewer have had their mechanism of action described.

One such oil is tea tree oil, currently enjoying a renaissance in popularity as a topical antimicrobial agent. Recent studies have shown it to be effective *in vitro* against a variety of organisms, including methicillin resistant *Staphylococcus aureus* (MRSA) [10], various skin colonising Gram-negative bacteria [11] and a wide range of fungi [12]. Early small clinical trials showed much promise for the eradication of MRSA carriage [13] and the treatment of cold sores [14]

While tea tree oil is a complex mixture of terpenes and several other components, this complexity suggests that resistance is unlikely to emerge. Finally, attempts at deducing a mechanism of action have shown that tea tree oil compromises the bacterial cytoplasmic membrane [15].

Conclusion

Thus there is good evidence that the use of many traditional therapies can be justified on scientific and clinical grounds. Many patients believe, quite often correctly, that alternative or complementary therapies have less side effects than conventional antimicrobials. Certainly, they appear less likely to promote antibiotic resistance. The scientific community has a responsibility to not dismiss such therapies until they have been investigated adequately.

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