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The potential role of garlic (*Allium sativum*) against the multi-drug resistant tuberculosis pandemic: a review

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Summary. Worldly data show the increasing incidence of *Mycobacterium tuberculosis* (MTB) and particularly of multi-drug resistant tuberculosis (MDR-TB). In developing countries, TB control programmes are overwhelmed by the complexity of treating MDR-TB infected people, as current tools and therapies are inadequate. MDR-TB could become the main form of TB. Risk factors that make South Africa into one of the main epicentres are analysed. A review of the studies carried out about antitubercular properties of *Allium sativum* both *in vitro* and *in vivo* is provided. The researches about the garlic extracts effectiveness against clinical isolates of MDR-TB are of scientific importance. *Allium sativum* offers a hope for developing alternative drugs. The involvement of traditional healers (TH) in the TB health management could facilitate the administration of garlic extracts to the infected patients.

Key words: tuberculosis, multidrug-resistant tuberculosis (MDR-TB), *Allium sativum*, traditional healers (TH), South Africa.

Riassunto *(Il ruolo potenziale dell'aglio, Allium sativum, nella tubercolosi farmaco-resistente: una rassegna)*. I dati a livello mondiale mostrano la crescente incidenza del *Mycobacterium tuberculosis* (TB) e in particolare della TB farmaco-resistente (MDR-TB). I programmi di controllo della TB nei paesi in via di sviluppo sono sopraffatti dalla complessità del trattamento per le persone colpite dalla MDR-TB, considerata l'inadeguatezza degli attuali strumenti e terapie. La MDR-TB può divenire la forma principale di TB. Sono analizzati i fattori di rischio che rendono il Sud Africa uno dei maggiori epicentri. Viene fornita una rassegna degli studi condotti sull'attività antitubercolare dell'*Allium sativum* sia *in vitro* che *in vivo*. Le ricerche sull'efficacia degli estratti d'aglio su campioni clinici di MDR-TB sono di interesse scientifico. L'*Allium sativum* offre una speranza per lo sviluppo di farmaci alternativi. Il coinvolgimento dei guaritori tradizionali nei programmi sanitari per la TB può facilitare la somministrazione di estratti d'aglio alle persone contagiate.

Parole chiave: tubercolosi, tubercolosi resistente (MDR-TB), *Allium sativum*, guaritori tradizionali, Sud Africa.

INTRODUCTION

Tuberculosis (TB) is caused by *Mycobacterium tuberculosis* (MTB) and is a global health issue, being a threat to the entire mankind, especially for the rapid increase of multidrug-resistant (MDR) MTB strains. Population mobility is one of the main factors of the disease fast spreading. Co-infection with the human immunodeficiency virus (HIV) poses a major health and scientific challenge, due to the high mortality associated.

The magnitude of the MDR-TB infection in some epicentres highlights the urgency of finding new medicines that could overcome the problem of drug resistance. Focus has now shifted to development of compounds from natural sources that have antimycobacterial activity. Garlic (*Allium sativum*) is a plant used as a food as well as a folk medicine for centuries by different cultures. It has shown to have a variety of pharmacological properties like antimicrobial, anticancer, antioxidant and many other effects. The present paper offers a review of *Allium sativum* activity against TB and MDR-TB, willing to contribute to the discussion about low-cost and affordable treatments.

Allium sativum represents an opportunity to develop innovative programmes and to reengage with planners about sustainable health policies in the poor settings where MDR-TB is nowadays out of control. Considering the social and financial costs of MDR-TB spread, the demonstration of the clinical efficacy of *Allium sativum* is needed. Till now reviews have shown that clinical trials have been few, small and inadequately controlled. However, the standardization and regulation of garlic as medicine – since thousands of years of expe-

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rience – may provide huge benefits for the TB containment. Scientific evidence from randomized clinical trials can support the use of *Allium sativum* and enhance access for MDR-TB infected people, through the public health system. Its use can allow an effective MDR-TB management, due to its affordability and the absence of toxic effects. Health expenditure might diminish substantially and Governments may be enabled to face the burden of the pandemic.

DATA ON GLOBAL TUBERCULOSIS SPREAD

Tuberculosis in the world

TB is a common infectious disease caused by various strains of mycobacteria, usually *Mycobacterium tuberculosis* in humans. One third of the world's population is thought to be infected with MTB and about 80% of the population in many Asian and African countries are tuberculin skin test positive. In 2009, 9.4 million of people were infected worldwide [1].

The resurgence of TB resulted in the declaration of a global health emergency by the World Health Organization (WHO) in 1993 [2]. In 2007, WHO estimated 13.7 million chronic active cases, 9.3 million new cases, and 1.8 million deaths, mostly in developing countries [3]. Most of the TB cases occur in Asia and Africa and the countries with the highest rates of TB incidence are India, China and South Africa [4].

There is evidence that human immunodeficiency virus (HIV) infection is correlated with increased risk of TB infection. The probability raises, in fact, 5-10 times in HIV-positive people [5].

MDR-TB is defined as resistance at least to the two most effective first-line TB drugs *i.e.* isoniazid (INH) and rifampicin (RMP). Outbreaks of MDR-TB were reported in US and Europe in patients with HIV infection, since the early 1990s [6].

The Report of WHO 2010 estimates 440 000 MDR-TB cases worldwide and 150 000 deaths in 2008 [7]. Only 7% of the estimated 440 000 cases of MDR disease were reported to WHO in 2008 and of these, only a fifth were treated [8]. According to WHO, Asia, countries of the former Soviet Union and East Europe are facing a serious and widespread MDR-TB epidemic; some provinces in China reported the highest rate of resistance, followed by India.

Direct transmission of MDR and XDR (extensively drug resistant)-TB, the last one caused by MDR strains also resistants to a fluoroquinolone and an injectable drug (kanamycin, amikacin, capreomycin), occurs frequently among individuals with no prior history of TB, as it was observed in Shanghai (March 2004 to November 2007) [9] and Western Cape in South Africa (September 2000 to August 2002) [10].

Although previously the MDR-TB epidemic was largely confined to east Asia and eastern Europe and the acquired immunodeficiency disease (AIDS) epidemic was mostly focused in sub-Saharan Africa, these infections are now clearly converging on both continents. TB patients with HIV have been shown to be twice as likely to get MDR-TB as people who are not HIV-positive. The HIV/TB co-epidemic represents a setback to global control of TB, which would otherwise be more manageable [11].

HIV and tuberculosis co-infection in sub-Saharan Africa

Mining in southern Africa has amplified HIV and TB epidemics across sub-Saharan Africa through social, political, and biological risks posed to miners and their communities [2]. The scale of international migration involves migrants from Botswana, Lesotho, Mozambique, Swaziland, Zimbabwe to work in the south African mines and through oscillating migration causes HIV/TB transmission in home regions [13].

In sub-Saharan Africa, mineral miners have among the highest TB incidence rates in the world. The mining industry in southern Africa may be implicated in as many as 760 000 new cases of TB each year, due to factors such as silica dust in mines, crowded living conditions, and the HIV infection. Through a multivariate analysis in 44 countries in sub-Saharan Africa, the same researchers found that, in high HIV prevalence settings, a huge mining sector represents a key factor in the spreading of TB [14].

Autopsies of black miners in South Africa reveal very high rates of silicosis and TB undetected or poorly-treated, rising from about 5% active pulmonary TB at autopsy in 1975 to 40% in 2008. Data on prevalence of silicosis in 2008 showed that one-quarter of all miners were affected by TB. Autopsies attested a gradual increase in the prevalence (per 1000) of active TB from 33 in 1975 to 50 in 1990, and a marked increase to 359 in 2008 [15].

Because of their multiplicative interactions, HIV and silicosis have an even larger effect on TB risk [16]. Studies in the gold mines show that, in addition to dramatic raise of TB in HIV-positive miners, there is increased incidence in HIV-negative miners [17, 18]. Seasonal migration makes the diagnosis more difficult. Even though TB is detected, in the miner's villages the chance of treatment interruption and failure raises, due to lack of appropriate health structures and of drugs supply. This factor leads to an increase of people developing drug-resistant forms of TB.

HIV and TB in South Africa: a severe threat to the global health

South Africa is one of the world's fastest growing tourist destinations, attracts millions of seasonal workers from neighbouring countries, and its ports and roads service several other African countries. A study conducted in a rural area in Kwazulu Natal investigated on a sample of 1539 patient during the period from January 2005 to March 2006. They found that 475 were culture-positive for TB and 39% of them (185 patients) were infected with MDR-TB, 6% (30 patients) had XDR, and all patients with XDR tuberculosis were co-infected with HIV [19]. Besides the

rapid raise of MDR and XDR-TB and the spreading of HIV, cumulatively, all these factors make for a potentially explosive international health crisis [20].

Tuberculosis in Europe

The European Centre for the Disease Prevention and Control (ECDC) and WHO Report of 2008 have found that, in that year, 82 611 cases of TB occurred in European Union (EU) countries. Almost a quarter of them were born in other countries, more than 60% being from Asia and Africa. 28 295 cases of those occurred in EU in 2008, were MDR-TB [21]. In 2009, 79 665 TB cases were reported by all 27 EU countries and MDR remains most frequent in Estonia, Latvia, Lithuania and Romania [22].

Instead in the European Region as a whole, in 2008 461 645 cases of TB were described (52.2/100 000), representing 6% of the global incidence of the disease. Eighteen of the 54 European countries are classified as high priority countries (HPC) because they constitute 87.6% of all the cases in the Region. In 2008 329 391 new episodes of TB and 46 241 deaths from TB were reported, the majority of them in the 18 HPC. 42% of the new infections occurred in the 15-44 age range [23]. In the same Region, MDR has resulted in more than 13 500 new and previously treated cases that defaulted from treatment. In a research it was observed that the strongest independent risk factors of death were advancing age and MDR, although male sex, European ethnicity, pulmonary TB and country of report also showed significant association [24].

Those data highlight the fact that MDR-TB is a threat to the European health stability.

Tuberculosis in Italy

In Italy, in the last 25 years, an increasing trend has been observed after an incidence decrease from the '50s to the '80s. Although Italy is classified as a low epidemical country, there is a significant concentration of cases among specific age ranges and at-risk groups and the insurgence of varying strains of MDR and XDR-TB [25].

In the decade 1998-2008 the incidence of TB increased (< 10/100 000 residents) with a total of 4500 cases per year. In 2008 4418 cases of TB occurred, 73% of which in the Northern and Central Italy. The TB rate among immigrants has doubled in the last decade, representing the 50% of total cases. The high incidence in foreign population depends both on the endemic situation in their countries and on the vulnerable status of the "immigrant" [26]. According to G. Besozzi, 5000 TB cases per year is an underestimation, as the real figure may be almost 8000 cases per year [27].

CURRENT MANAGEMENT STRATEGIES

Considerations

The WHO strategy with directly observed treatment short-course (DOTS) is a standardized therapy with supervision and patient support provided by a health worker. The care-giver is responsible to administer the drugs to TB patients and to ensure their adherence [28]. That approach was effective for the treatment of TB.

However, MDR-TB presents new challenges. MDR strains could become the main form of TB, since subpopulations of resistant mycobacteria can emerge as the dominant strain in the presence of drug-selection pressure. Management of MDR-TB is more complex, costly, time-consuming and less effective than it is for drug-susceptible TB [29]. In developing countries, it would be unwise to rely on existing technologies alone. Most MDR-TB programmes in the resource-poor settings do not have access to the complex and expensive diagnostics and they face constraints like worldwide shortages of quality-assured second-line drugs (SLD) [30].

Lastly, the management of the debilitating and toxic side-effects of drugs combination for MDR-TB and HIV requires alternative therapies. Studies have shown higher rates of adverse reactions in HIV-infected patients to the anti-TB therapy rifampicin [31]. One of the principle drugs for HIV treatment, efavirenz, may, in fact, cause toxic interaction with rifampicin [32]. The most common side effects noted – due to drugs interactions and toxicity – were peripheral neuropathy (PN), rash, gastrointestinal upset (GI), hepatitis and neurological events [33].

Moreover, strains of TB resistant to all major anti-TB drugs have emerged in Central Asian countries [34]. Drug resistance severely threatens TB control, since in the medium period existing drugs could be no longer effective. If no new antituberculosis drugs are found, returning to the preantibiotic era could be a reality [35].

Research efforts in affordable treatments that work faster, with less side-effects and compatible with medications for HIV must be prioritized, as current tools and drugs are inadequate [36].

Tuberculosis treatment costs

DOTS-Plus is a case-management strategy designed by WHO to manage MDR-TB using SLD. However the following examples show that costs are not sustainable:

- in the period between 1999-2002, in Manila, the average cost per patient treated in the DOTS-Plus project was US$ 4192, of which US$ 3355 for health system costs and US$ 837 for costs incurred by patients and their families to benefit from therapies [37];
- drug costs for the 30 000 estimated cases of MDR-TB in the Russian Federation in 2003 could amount to US$ 70 million at highly-concessionary Green Light Committee (GLC) prices, and US$ 452 million at market prices. In 2003, in the Russian Federation the average cost per patient treated was US$ 10 319 for DOTS-Plus [38];
- in 2006-8, Médecins sans frontières (MSF) have spent in Armenia € 9000 per patient for treatment and SLD; they have paid around US$ 7300 per MDR-TB patient in Cambodia [39].

To achieve universal access to treatment recommended in the Global Plan to Stop TB, 1.4 million cases of MDR-TB in the 27 countries with the highest burden of MDR disease will need to be cured [40]. The total estimated cost of such treatment for 2010-2015 is US$ 16.2 billion, an amount far in excess of the existing level of funding [41].

In developing countries the charge for treatment of MDR and XDR cases may far exceed their total budgets for health care [42]. Health services costs cause both impoverishment of households that fall into debt to seek services or exclusion of others from health care access. In countries with high rates of poverty, huge rates of catastrophic spending are expected [43].

THE ANTITUBERCULAR ACTIVITY OF GARLIC (*ALLIUM SATIVUM*)

Allium sativum *properties*

Garlic (*Allium sativum*) is world famous from centuries for its contribution to human health. Literature says that garlic has originated in Central Asia and then spread to remaining parts of world [44]. Garlic was known to Chinese health providers before 3000 BC and is a part of Chinese diet and traditional medicine till today. It was also known to Egyptians, Greeks, Romans and Africans from ages and was used as a treatment for several ailments. Hippocrates (470-358 BC) has recommended its use in treating infections [45]. Besides, according to the Unani and the Ayurvedic systems of medicine, garlic is a well-known remedy for several diseases [46]. *Allium sativum*, in fact, has been found to exhibit in vitro i) antimicrobial activities against Gram-positive and Gram-negative bacteria, including species of *Escherichia, Salmonella, Staphylococcus* and *Streptococcus, Klebsiella, Proteus, Bacillus, Clostridium, Helicobacter pylory and even MTB* ii) antifungal activity - particularly against *Candida albicans* – iii) antiparasitic and iv) antiviral action [47-48]. It has *in vitro* a strong anticancer effects [49-54] as well as anti-inflammatory, immunomodulatory and antioxidant properties. It also possesses antihyperlipedemic, antihelminthic, antihypercholesterolaemic, antihypertensive activity [55].

Researchers have found garlic to be effective *in vitro* against several opportunistic infections in acquired immunodeficiency disease (AIDS), including candidiasis [56], herpes and *Cryptococcus* infections, as well as *Cryptosporidium, Cytomegalovirus* [57] and *Pneumocystis carinii* [58]. According to Cutler and Wilson, allicin liquid extracts were highly active against clinical isolates of multiple antibiotic resistant *S. aureus*, as "allicin is considered to be the most potent antibacterial agent in crushed garlic extracts" [59]. However, undamaged garlic bulb contain not allicin but alliin which is converted into allicin enzimatically when fresh garlic is squeezed [60].

Wills reported that allicin is an inhibitor of sulfhydryl metabolic enzymes and suggests that its antimicrobial properties are due to specific interaction with SH- group [61]. It is now recognized that the wide-spectrum antimicrobial activity of allicin is due to the multiple inhibitory effects it can had on various thiol-dependent enzymatic systems, its main antimicrobial effect remaining its interaction with important thiol-containing enzymes [62].

Allium sativum and tuberculosis

In developing countries current tools and drugs for MDR-TB are inadequate and the treatments available are not only unsustainable but cause either several side effects. In view of the increased incidence of MDR-TB, the research of new antitubercular drugs based on affordable and more effective treatments has already begun. Studies on innovative alternative plant extracts of medicinal value need to be emphasized, as plants are an important source of new antimicrobial agents, with little toxicity, able to replace drugs to which mycobacteria resistance has occurred [63].

As *Allium sativum* is concerned, the *in vitro* tests undertaken about the inhibitory effect on MDR-TB are at an advanced stage whereas few researches *in vivo* have been conducted.

First studies on the antitubercular treatments with Allium sativum

A review of the main studies that tested garlic as an antitubercular therapy is provided below.

In 1912, Dr. WC. Minchin, of the Kells Union Hospital in Ireland, published *Allyl Sufphide in the treatment of Lupus and tuberculosis* [64]. He described an inhaler mask containing a sponge soaked in garlic juice for the TB treatment. Inhaled garlic juice would function as a volatile germicide, which would destroy the bacterium. Cases of those recorded by Dr. Minchin may be claimed as proof that in certain individuals the drug practically annihilates the activity of the bacterium [65]. Minchin gave also the simple recipe for a treatment of tuberculosis with oil of garlic, successful cure guaranteed within two months, even in far advanced cases [66].

In the same year, Ballière affirmed: "..there is no doubt that allyl sulphide in the juice of garlic is quite a good chemotherapeutic agent, for sulphur…turns the toxin of microbes into harmless toxoid" [67].

In 1914, the inhibitory effect of garlic on mycobacteria was reported by Dr. MW. McDuffie of the Metropolitan Hospital in New York. He compared garlic with 55 other treatments for TB and concluded that it was the most effective. He affirmed "Garlic contains a volatile oil, called allyl sulphide, and its medical properties depend on this oil, strongly antiseptic, it seems to have a remarkable power of inhibiting the growth of the Koch's bacillus, eliminated by the lungs, skin, kidneys and liver, and oxidizes into sulphonic acid in the system. Applied locally, it is freely absorbed by the skin and penetrates the deeper tissues. Garlic gave us our best results, and would seem equally efficacious, no matter what part of tile body affected, whether skin, bones, glands, lungs or special parts" [68].

Researches about the inhibitory effect of Allium sativum *extracts against* Mycobacterium tuberculosis

Cavallito and Bailey first isolated and identified, in 1944, the component responsible for the broad-spectrum antibacterial activity of crushed garlic cloves. The compound turned out to be an oxygenated sulphur compound which they termed allicin [69]. By steam distillation of ethanolic garlic extracts, the researchers obtained a colourless strong-smelling oil which was active against a wide range of bacteria, in concentrations as low as 1:85 000. Two years later, Rao and coworkers demonstrated, for the first time, the *in vitro* inhibitory effect of allicin on the growth of *Mycobacterium tuberculosis* (MTB) [70].

The study by Rao was confirmed and extended by Delaha and Garagusi (1985). They established evidence of inhibitory concentration of allicin on 17 species of mycobacteria. The concentration of garlic extract required was in the range of 1.34-3.35 mg/mL suggesting that there is only a slight variation in the susceptibility of the strains to allicin [71].

The antituberculosis activity *in vivo* of garlic oil preparation was demonstrated in a study by Jain (1993) where guinea pigs were given an intraperitoneal dose of 0.5 mg/kg [72]. Jain (1998) observed in tubercle bacilli-exposed guinea pigs, treated with streptomycin or garlic oil, a comparable marked epithelioid reaction. However, when garlic oil was used, a reduced caseative process was noted in the organs involved, indicating that garlic oil administration causes less marked lesions in the viscera of the animals inoculated with tubercle bacilli [73].

The high potential of garlic extract, was revealed by the discovery (1996), based on a previous investigation [74], that it was able to inhibit the growth of *Mycobacterium tuberculosis* $H_{37}R_v$ and *Mycobacterium tuberculosis* TRC-C1193, susceptible and resistant to isoniazid (first-line antituberculosis medication), respectively. The minimum inhibitory concentration (MIC) was between 80 and 160 μg/ml for the susceptible strain and between 100 and 200 μg/ml for the resistant strain. In addition, water extract of garlic was proven to be able to inhibit the incorporation of ^{14}C glycine into whole cells, indicating that the primary mechanism of action is by inhibition of protein synthesis [75]. In a further study, Murthy *et al.* (1997) showed that higher purification of allicin gave a chloroform elutable fraction called CEF-allicin, which inhibited the growth of both the susceptible and the isoniazid resistant strains of TB with a lower minimum inhibitory concentration (MIC) *i.e.* 25 μg/ml. The authors, in view of the increased incidence of TB caused by MDR strains emphasize the need for the development of new antitubercular drugs, preferably with structure different from that of the existing ones and active against MDR-TB. They found that CEF-allicin together with trifluoperazine (TFP) possess the advantage of being active against *M. avium,* which causes disseminated infections in AIDS-patients being potential antitubercular drugs [76].

In 2006, according to a research – that joined the University of Aligarh in India and the University of Cleveland in US – allicin was proved to be a potential agent to counteract TB infection, via a potent anti-inflammatory effects on host mononuclear cells infected with MTB. Allicin, in fact, increased the activity of the enzyme glutathione peroxidase thus decreasing the production of reactive oxygen species and finally lowering the production of inflammatory mediators [77]. This phenomenon was reported to be due to the suppression of antigen 85B transcription at both gene and protein level. Antigen 85B is abundantly secreted by MTB and is responsible of the induction of the inflammatory madiator TNF-alpha. Suppression of 85B expression by allicin seems to be mediated via inhibition of glutathione. Therefore the researchers suggested that the garlic compound should be tested in vivo models to evaluate its therapeutic potential in the pathogenesis of tuberculosis [78].

An interesting *in vitro* test about the antitubercular activity of *Allium sativum* was performed in Nigeria (2010), where the extract of *Allium sativum* was expressed as disc diffusion method and compared with standard antibiotics. The antitubercular activity of garlic on multiple-drug resistant Mycobacterium was investigated among Nigerian HIV-infected-persons and it exhibited maximal activity against all isolates even at reduced concentrations with inhibitory zone diameter (IZD). Only two of the standard antitubercular antibiotics used, streptomycin and rifampicin, showed significant activity against isolates tested [79].

Researches about Allium sativum *extracts and MDR-TB isolates*

The antitubercular activity of garlic extracts become particularly interesting in the case of MDR-TB. In fact, some years ago Dr. R. Cutler and Dr. P. Wilson, at the Royal London Hospital, noted that a number of strains of MDR-TB isolated from patients grew on all slopes where strains were treated with streptomycin, while the same isolates were completely inhibited by allicin liquid [80]. Two studies published some years later demonstrated the inhibitory effects of allicin against both, non-MDR and MDR isolates of *M. tuberculosis*. In 2010, the research by Gupta, *et al.* was carried out to evaluate the antitubercular activity of aqueous extracts of five medicinal plants. Water extract of *Allium sativum* was found to have activity against two MDR *M. tuberculosis* isolates that were found to be resistant against rifampicin and isoniazid [81]. A study by Hannan *et al.* (2011) was undertaken to evaluate the antibacterial activity of garlic against non-MDR and MDR isolates of *M. tuberculosis*. A total of 20 clinical isolates of MTB including 15 MDR and 5 non-MDR were investigated. Ethanolic extract of garlic was prepared by maceration method. MIC of garlic extract was ranged from 1 to 3 mg/mL, showing inhibitory effects of garlic against both non-MDR and MDR *M. tuberculosis* isolates [82].

The above research about the garlic extract effectiveness against clinical isolates of MDR *M. tuberculosis* is of high scientific interest, since garlic extract may both reduce the scale of MDR-TB and decrease the public health budget necessary for the management of the disease.

Synergistic effect of current antimycobacterial agents and garlic extracts: a likely integration

The synergistic effect of garlic crude extract with the conventional therapies represents a challenging research area.

In 1999, this result was demonstrated in a study on 30 patients suffering of tubercular lymphadenitis. Two groups of patients, 30 each, were given for 30 days antitubercular therapy (ATT), consisting of isoniazid, rifampicin, ethambutol and pyrazinamide. For the next 15 days some patients of group 1 received 3-6 garlic pearls in addition to ATT, while other patients received ATT only. From 46th day onwards both the groups received ATT only, for 6-8 months. In the serum samples collected on the 45th day, the patients who received garlic pearls showed significantly much higher antitubercular activity than the others, suggesting a good potential as antitubercular drug for garlic, even when given as a supplement to ATT [83].

In the same vein, a research (2010) demonstrated that crude aqueous extract (CGE) of garlic inhibited the growth of MTB *in vitro*. Moreover, MIC of isoniazid and rifampicin were significantly reduced by addition of crude aqueous extract of garlic in the media [84].

PLANNING FOR TB PREVENTION AND CURE WITH *ALLIUM SATIVUM*

Garlic potential use against tuberculosis

At least two thirds of the world population rely on medicinal plants as their primary source of medicinal treatment. In view of the relevance of traditional medicine (TM), WHO has set a strategy that involves four objectives: integration of TM with national health care systems; promotion of the safety, efficacy and quality; increasing the availability and affordability of TM; promotion of effective TM by providers and consumers [85].

Garlic is a common ailment worldwide cultivated with several properties and tremendous curative potential. Used for ages in culinary and medical traditions, its regular intake has shown beneficial effects on the immune system.

Allium sativum has already been screened for pharmacological activity. Further investigations are needed for its development as a drug for TB treatment. Once conducted the necessary clinical trials to assess *Allium sativum* efficacy as antitubercular drug for humans, it may be administrated:

- as a preventive medicine for TB infection;
- as a monotherapy cure for TB and MDR-TB, upon further studies to assess specific doses required;
- added to ATT to strengthen the efficacy of the therapy and reduce its side-effects.

During the past three decades, pharmaceutical companies and research scientists have shown an increased interest in phytomedicine. The pressing need for anti-TB drugs, affordable by the majority of people, finds in medicinal plants a potential solution [86]. As garlic is broadly cultivated worldwide and can be easily manufactured, the suggested approach seems more sustainable and appropriate for the poor settings than the conventional one.

Traditional healers involvement

An additional convincing advantage of using garlic extract in developing countries is that diseased people can count on their own traditional healers (TH), who provide care services informally within the solidarity net of the community.

According to the South African Department of Health, traditional health practitioners are an essential component of the comprehensive care delivered. Indeed they tend to adopt an holistic approach to health promotion and diseases management. A study found that in urban areas in Kwazulu Natal patients interviewed used to consult TH regularly, as they could share a common cultural belonging [87].

The potential role for collaboration between the health service and TH, especially as TB treatment supervisors, has been investigated. A research reported that 84% of the 100 TB patients interviewed would consider choosing a TH as treatment supervisor and 92% of TH were willing to act as supervisor. Thus, potential for collaboration and interaction with the formal TB care-givers was found in the setting observed [88]. TH when integrated into the existing community-based TB DOTS programme made an effective contribution to TB plan performance, as examined in a pilot scheme in a Kwazulu Natal district [89]. Some TH interviewed in Malawi claimed to know about TB. The study remarks also the importance of involving TH in the national TB control programme of Malawi [90].

There is a large literature discussing the potential for cooperation between TH and conventional health services. Sources note that the majority of people in Africa are believed to attend TH prior to, or in parallel with conventional health services [91-92]. The role they can play in TB control programme could be significant, as TH are relevant members of local society and deeply integrated as well as largely appreciated by their communities for medical issues.

The solution could be at the same time affordable and efficient.

CONCLUSION

Tuberculosis is the leading cause of death worldwide, claiming the major number of adult lives in combination with AIDS. Pulmonary TB is a very contagious disease, and it spreads easily especially in poor and crowded contexts. The resistant strain (MDR-TB) is even more

threatening and poses a significant challenge to national healthcare systems. Failure to prevent further convergence of the HIV infection and MDR-TB epidemics will be catastrophic for many countries in the years to come [93].

With limited financial resources for diseases control, planning should take into consideration all the available means. According to Dr. Raviglione (WHO, Director of the Stop TB Department), "Shorter treatment regimens and more effective MDR-TB care regimens are priorities for drug development. An ideal candidate would shorten the treatment from the current six months to less than two months; have a novel mechanism of action; not interact with anti-retrovirals; be taken orally once daily or intermittently; and be low in cost" [94].

With the urgent need for new anti-TB agents, it is appropriate to further investigate the antimycobacterial activity of *Allium sativum*.

Considering the social and economic costs of MDR-TB spread, any clinical trials with Allium sativum might contribute to the Global health and diminish substantially the Governments' health expenditure, necessary to face the burden of the pandemic.

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Conflict of interest statement

There are no potential conflicts of interest or any financial or personal relationships with other people or organizations that could inappropriately bias conduct and findings of this study.

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