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3.4.4: BOOKS AND CHAPTERS IN EDITED VOLUMES/BOOKS PUBLISHED BY TEACHERS

- **2015-16 (10)**

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S.K. Deshmukh • J.K. Misra
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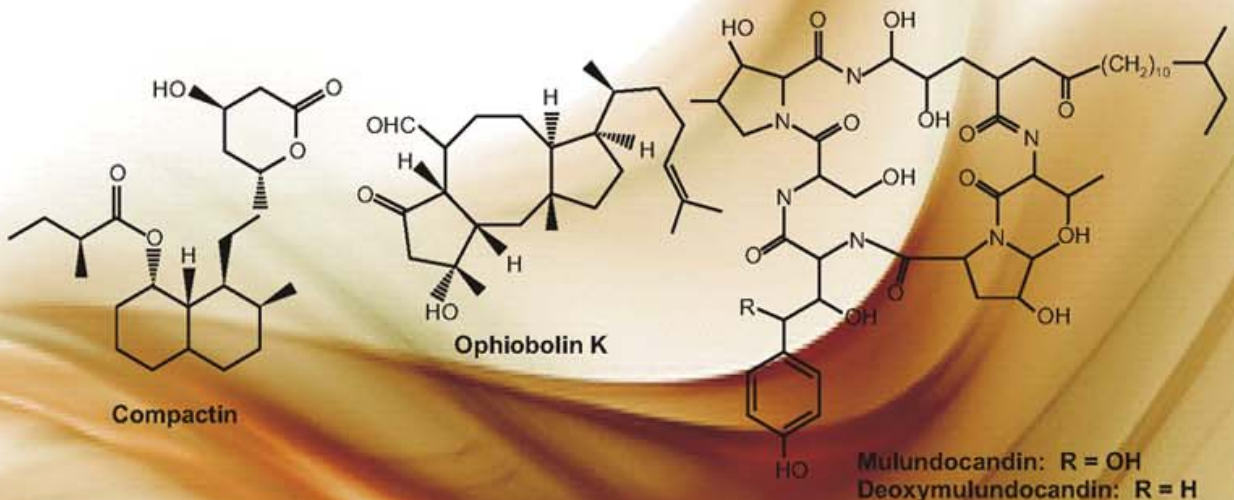

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FUNGI

Applications and Management Strategies

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CRC Press
Taylor & Francis Group
Boca Raton London New York

CRC Press is an imprint of the
Taylor & Francis Group, an **informa** business

A SCIENCE PUBLISHERS BOOK

CRC Press
Taylor & Francis Group
6000 Broken Sound Parkway NW, Suite 300
Boca Raton, FL 33487-2742

Printed on acid-free paper
Version Date: 20160115

International Standard Book Number-13: 978-1-4987-2491-3 (Hardback)

Library of Congress Cataloging-in-Publication Data

Names: Deshmukh, S. K. (Sunil K.), editor. | Misra, J. K., editor.
Title: Fungi / editors: Sunil Kumar Deshmukh and J.K. Misra.
Description: Boca Raton, FL : CRC Press, Taylor & Francis Group, 2016. |
Includes bibliographical references and index.
Identifiers: LCCN 2015047485 | ISBN 9781498724913 (hardcover : alk. paper)
Subjects: LCSH: Fungi.
Classification: LCC QK603 .F958 2016 | DDC 579.5--dc23
LC record available at http://lccn.loc.gov/2015047485

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Contents

CHAPTER 3

Antimycobacterials from Fungi

Sunil Kumar Deshmukh,[1,*] *Shilpa Amit Verekar*[2] and *B.N. Ganguli*[3]

ABSTRACT

Tuberculosis is an endemic disease of the poverty ridden, undernourished and over populated countries of the world. It is also a systemic disease that is extremely dependent on the physiology of the system it invades and thus varies significantly from person to person. New developments in the treatment of this disease have rarely percolated down to the larger sections of the under privileged in our societies. The need for highly active, long acting, yet less expensive drugs against Multi-Drug Resistant (MDR) *Mycobacterium tuberculosis* still exists. Research initiative on endophytic fungi as a source of such biotherapeutics is an important step that could help to tackle the need. Complete eradication of tuberculosis is certainly possible by integration of research results and public health programs. However, such initiatives have been hindered by the lack of effective communication lines in many countries of the world. Language is just one of the several hurdles! Nationalistic jingoism is another!!

A major initiative could be to investigate the effects of the mixtures of compounds already known to have activities against different strains of *M. tuberculosis*. Such as, those reported in the local knowledge forums of Ayurvedics in villages of India and in allopathic medical publications. We must have a "United Front to Combat Tuberculosis" (UFCT)—A Worldwide Effort.

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Introduction

In the many countries of the world, the hunt for new anti-mycobacterial compounds is going on. In most of them, a marker MIC level is set so that both synthetic and natural (plants, fungal) compounds can be selected that have better therapeutic potential especially against clinically relevant Multi Drug Resistant strains of *Mycobacteria.* The marker compounds used are Isoniazid with a Minimum Inhibitory Concentration (MIC) of 0.04–0.09 µg/mL and Kanamycin sulphate with an MIC of 2.0–5.0 µg/mL usually. In the opinion of the authors, the use of selective mixtures of anti-tubercular compounds could be better, so that development of resistance is slowed down if not totally prevented. Choice of several different mixtures of compounds could be of advantage after extensive evaluation. Serum binding may not be a disadvantage if a slow but continuous release is observed and measured over time. What needs also to be borne in mind is that this chronic disease usually affects the poorer populations of the world where public health efforts are negligible, if not totally absent, and communications extremely difficult.

Scrutiny of the available literature of the years from 2002 to 2013 clearly indicated that research initiatives against *M. tuberculosis* are discouraging with the publication of 1–2 papers on anti-mycobacterial per year. Moreso, to our utter surprise, during the year 2006–2007 there was no report in the journals we reviewed. But in the year 2010 the largest number of publications appeared. This poses a million dollar question. What made the researches to jump on it too heavily and suddenly? But this momentum is a welcome move.

The World Health Organization (WHO) estimated that currently ca. 50 million people were infected and 1500 people dieper hour from Tuberculosis worldwide. After the detection of strains of *Mycobacterium tuberculosis* resistant to multiple drugs (MDRTB), the search for new antimycobacterials has been intensified (WHO, 2008). The world recognizes medicinal plants as repositories of fungal endophytes that produce metabolites with novel molecular structures that are active against various human diseases. For example, extracts of endophytic fungi isolated from Thailand's Garcinia plant species inhibit *M. tuberculosis* (Wiyakrutta et al., 2004). Several compounds reported from fungi with anti-mycobacterial activities are shown in Table 1.

Antimycobacterials from Fungi

From Ascomycetes

3-Nitropropionic acid (3-NPA) **(1)** (Fig. 1) is found in the extracts of several strains of endophytic genus *Phomopsis* sp. It is highly active against *M. tuberculosis* H37Ra with an MIC of 3.3 µM, but no *in vitro* cytotoxicity was seen in a number of cell lines. Endophytes produce high levels of 3-NPA which accumulates in certain plants and could, therefore be a marker

Table 1. Antimycobacterial from fungi.

Sr. No.	Fungus	Source	Compounds Isolated	Biological Activity*	Reference
1.	*Phomopsis* sp.	*Urobotrya siamensis*, *Grewia* sp., *Mesua ferrea*, *Rhododendron lyi*, *Tadehagi* sp., *Gmelina elliptica*	3-Nitropropionic acid (3-NPA) **(1)**	Compound **(1)** inhibits *Mycobacterium tuberculosis* H37Ra strain (MIC of 3.3 µM). Inhibits the isocitrate lyase (ICL), the enzyme involved in fatty acid catabolism and virulence in *M. tuberculosis*	Chomcheon et al., 2005 Munoz-Elias et al., 2005
2.	*Nodulisporium* sp.	Marine derived fungus	Vermelhotin **(3)**, Aspergillusidone D **(4)**	Vermelhotin **(3)** inhibits five reference strains of *M. tuberculosis* with MICs of 3.1–6.2 µg/mL. Aspergillusidone D **(4)** has an MIC value of 50.0 µg/mL	Kasettrathat et al., 2008; Ganihigama et al., 2015
3.	*Phomopsis* sp. BCC 1323	Leaf of *Tectona grandis* L.	Phomoxanthones A **(5)** and B **(6)**	Compounds **(5)** and **(6)**, *M. tuberculosis* H37Ra strain (MIC of 0.5 and 6.25 µg/mL respectively)	Isaka et al., 2001
4.	*Phomopsis* sp. PSU-D15	*Garcinia dulcis*	Phomoenamide **(7)**	Compound **(7)** *M. tuberculosis* (MIC of 6.25 mg/mL)	Rukachaisirikul et al., 2008
5.	*Diaporthe* sp. BCC 6140		Diaportheins A **(8)** and B **(9)**	Compound **(8)** inhibits *M. tuberculosis* (MIC 200 µg/mL) and Compound **(9)** at (MIC 3.1 µg/mL)	Dettrakul et al., 2003
6.	*Phoma* sp. NRRL 46751	*Saurauia scaberrinae*	Phomapyrrolidones B-C **(10-11)**	Compound **(10)** and **(11)** inhibits *M. tuberculosis* H37Pv (weak *in vitro* anti-tubercular activity when tested using the microplate Alamar Blue assay (MABA) for replicating cultures with MIC of 5.9 and 5.2 µg/ml respectively In the low oxygen recovery assay (LORA) with MIC 15.4 and 13.4 µg/ml respectively for non-replicating	Wijeratne et al., 2013

7.	Fruit hull of *Garcinia mangostana* L.		α-Mangostin **(12)**	-	Arunrattiyakorn et al., 2011
	Compound **(12)** Incubation with *C. gloeosporioides* (EYL131)		Mangostin 3-sulfate **(13)**, Mangostanin 6-sulfate **(14)**, 17,18-Dihydroxymangostanin 6-sulfate **(15)**, Isomangostanin 3-sulfate **(16)**	Compound **(12-13)** inhibits *M. tuberculosis* (MICs 15.24 and 6.75 µM respectively) Compound **14–16** (MIC > 50 µg/mL)	Arunrattiyakorn et al., 2011
	Compound **(12)** Incubation with *N. spathulata* (EYR042).		Mangostin 3-sulfate **(13)**	Compound **(13)** inhibits *M. tuberculosis* (MIC 6.75 µM)	Arunrattiyakorn et al., 2011
8.	*Chaetomium globosum* strain IFB-E036	*Cynodon dactylon*	Chaetoglocins A-B **(17-18)**	Compounds **(17-18)** inhibits *B. subtilis, Streptococcus pyogens, Mirococcus luteus* and *M. smegmatis* with MICs between 8 and 32 µg/mL	Ge et al., 2011
9.	*Chaetomium globosum* KMITL-N0802	Thai soil	Echinuline **(19)** and Chaetomanone **(20)**	Compounds **(19-20)** inhibits *M. tuberculosis* with MIC of 169.92 and 216.62 µM respectively	Kanokmedhakul et al., 2002
10.	*Chaetomium brasiliense*		Mollicellins K **(21)**	Compound **(21)** inhibits *M. tuberculosis* MIC 12.5 µg/mL	Khumkomkhet et al., 2009
11.	*Chaetomium cochliodes* VTh01 and *C. cochliodes* CTh05		Cochliodone C **(22)**, Chaetoviridine E and F **(23-24)**, Chaetochalasin A **(25)**, 24(R)-5α,8α-Epidioxyergosta-6-22-diene-3β-ol **(26)**	Compounds **(22–26)** inhibits *M. tuberculosis* (MICs 200, 50, 100, 100, and 200 µg/mL, respectively)	Phonkerd et al., 2008
12.	*Trichoderma* sp.	Marine sponge-derived fungus	Trichoderins A **(27)**, A1 **(28)**, and B **(29)**	Compounds **(27–29)** active against both dormant and multiplying *M. tuberculosis* strain H37Rv. *M. smegmatis*, *Mycobacterium bovis* BCG, and *M. tuberculosis* H37Rv with MIC values in the range of 0.02–2.0 µg/mL	Pruksakorn et al., 2010

Table 1. contd....

Table 1. contd....

Sr. No.	Fungus	Source	Compounds Isolated	Biological Activity*	Reference
13.	*Coniothyrium cereale*	Marine green alga *Enteromorpha* sp.	(–)-Trypethelone **(30)**	Compound **(30)** is active against *M. phlei*, *S. aureus*, and *E. coli*, at 20 µg/disk with inhibition zones of 18, 14, and 12 mm, respectively	Elsebai et al., 2011
14.	*Biscogniauxia formosana* BCRC 33718	*Cinnamomum* sp.	Biscogniazaphilones A **(31)** and B **(32)**, N-trans-feruloy-3-O-methyldopamine **(33)**, 5-Hydroxy-3,7,4-trimethoxyflavone **(34)**, 4-Methoxycinnamaldehyde **(35)**, Methyl 3,4-methylenedioxycinnamate **(36)**, 4-Methoxy-trans-cinnamic acid **(37)**	Compounds **(31)** and **(32)** inhibits *M. tuberculosis* strain H37Rv with MIC of ≤ 5.12 and ≤ 2.52 µg/mL, respectively Compounds **(33–37)** inhibits *M. tuberculosis* strain H37Rv with MIC of 12.5, 25.0, 42.1, 58.2 and 50.0 µg/mL, respectively	Cheng et al., 2012
15.	*Fusarium* sp. BCC14842	Bamboo leaf	Javanicin **(38)**, 3-O-Methylfusarubin **(39)**, a diastereomer of Dihydronaphthalenone **(40)** and 5-Hydroxy-3-methoxydihydrofusarubin A **(41)**	Compounds **(38)** and **(40)**, anti-mycobacterial activity (MICs of 25 µg/mL) Compounds **(39)**and **(41)**, anti-mycobacterial activity(MICs of 50 µg/mL)	Kornsakulkarn et al., 2011
16.	*Fusarium* sp.	Mangrove plant	Cadmium **(42)** and copper **(43)** metal complexes of Fusaric acid	Compounds **(42-43)** *M. bovis* BCG (MIC 4 µg/mL) and the *M. tuberculosis* H37Rv strain (MIC 10 µg/mL)	Pan et al., 2011
17.	*Fusarium* spp. PSU-F14	Sea fan-derived fungi	9α-hydroxyhalorosellinia A **(44)**, Nigrosporin B **(45)** anhydrofusarubin **(46)**	Compounds **(44-46)** inhibits *M. tuberculosis* H37Ra (MIC of 39, 41 and 87 µM respectively)	Trisuwan et al., 2010

18.	*Microsphaeropsis* sp. BCC 3050	Lichenicolous fungus isolated from *Dirinaria applanata*	3′-O-Demethylpreussomerin I **(47)**, Preussomerins E–I **(48–52)**, Deoxypreussomerin A **(53)** and Bipendensin (Palmarumycin C11) **(54)**	Compounds (**47–54**) inhibits *M. tuberculosis* H37Ra (MIC 25, 3.12, 3.12–6.25, 6.25, 12.5, 25, 1.56–3.12, 50 µg/mL, respectively)	Seephonkai et al., 2002
19.	*Phaeosphaeria* sp.		(3S,4R)-4,8-Dihydroxy-3-methoxy-3,4-dihydronaphthalen-1(2H)-one **(55)**, (4S)-3,4,8-Trihydroxy-6-methoxy-3,4-dihydronaphthalen-1(2H)-one **(56)**, (S)-4,6,8-Trihydroxy-3,4-dihydronaphthalen-1(2H)-one **(57)**, 1-(1-Hydroxy-3,6-dimethoxy-5,8-dioxo-5,8- dihydronaphthalen-2-yl) ethyl acetate **(58)**, 2,5,7-Trihydroxy-3-(1-(1-hydroxy-3,6-dimethoxy-5,8-dioxo-5,8-dihydronaphthalen-2-yl)ethyl)naphthalene-1,4-dione **(59)**, 6-Ethyl-5-hydroxy-2,7-dimethoxynaphthalene-1,4-dione **(60)**	Compounds **(55-56)** (*M. tuberculosis*) MICs 12.50 µg/mL, Compound **(58)** MIC of 12.50 µg/mL, compound **(59)**, MIC 0.39 µg/mL. Compound **(60)** MIC of 6.25 µg/mL, compound **(57)** MIC of 25 µg/mL.	Pittayakhajonwut et al., 2008
20.	*Dothideomycete* sp. LRUB20	*Leea rubra*	2-hydroxymethyl-3-methylcyclopent-2-enone **(61)**, Asterric acid **(62)**, and hydrazone derivative of cis-2-hydroxymethyl-3-methylcyclopentanone **(63)**	Compounds **(61–63)**, have mild anti-mycobacterial activities with MIC values of 200 µg/mL	Chomcheon et al., 2006
21.	*Penicillium dipodomyicola* - HN4-3A	Stem of the mangrove plant *Acanthus ilicifolius*	Peniphenone B **(64)**, Peniphenone C **(65)**	Compounds **(64)**, **(65)**, inhibited Mptp B with IC_{50} values of 0.16 ± 0.02 and 1.37 ± 0.05 µM, respectively	Li et al., 2014

Table 1. contd....

Table 1. contd....

Sr. No.	Fungus	Source	Compounds Isolated	Biological Activity*	Reference
22.	*Geotrichum* sp.	*Crassocephalum crepidoides*	7-butyl-6,8-dihydroxy-3(R)-pent-11-enylisochroman-1-one **(66)**, 7-but-15-enyl-6,8-dihydroxy-3(R)-pent-11-enylisochroman-1-one **(67)** and 7-butyl-6,8-dihydroxy-3(R)-pentylisochroman-1-one **(68)**	Compound **(66–68)** inhibits *M. tuberculosis* H27Ra. MICs are respectively, 25 µg/mL, 50 µg/mL, and inactive	Kongsaeree et al., 2003
23.	*Verticillium hemipterigenum*	Pathogenic fungus	Enniatins H **(69)**, I **(70)**, B **(71)**, and B4 **(72)**	Compound **(69–72)** inhibits *M. tuberculosis* H37Ra (MICs 3.12–6.25 µg/mL)	Nilanonta et al., 2003
			Analogues H, I and MK1688 **(73–75)**	Compound **(73–75)** (MICs 3.12–6.25 µg/mL)	Vongvilai et al., 2004
24.	Unidentified fungus		Enniatins L **(76)**, M1 **(77)**, M2 **(78)** and N **(79)**	Compound **(76–79)** MICs of 6.25–12.5 µg/ml	Vongvilai et al., 2004
25.	*Nigrospora* sp.	Mangrove endophyte	4-Deoxybostrycin **(80)** and Nigrosporin **(45)**	Compound **(80 and 45)** In the Kirby-Bauer disk diffusion susceptibility test, both had inhibition zone sizes of over 25 mm against *M. tuberculosis*	Wang et al., 2013
26.	*Hirsutella kobayasii* BCC 1660	Entomopathogenic fungus	Hirsutellide A **(81)**	Compound **(81)** *M. tuberculosis* H37Ra using the microplate Alamar Blue Assay (MABA) showed a MIC with 6–12 µg/mL	Vongvanich et al., 2002
27.	*Hirsutella nivea* BCC 2594	Pathogenic fungus	Hirsutellones A–D **(82–85)**	The compounds **(82–85)**, inhibits *M. tuberculosis* H37Ra (MIC 0.78, 3.125, 0.78, 0.78 µg/mL)	Isaka et al., 2005

28.	*Trichoderma* sp. BCC 7579		Hirsutellone F **(86)**, Hirsutellones A, B, and C	Compound **(86)** inhibits *M. tuberculosis* H37Ra (MIC 3.12 µg/mL)	Isaka et al., 2006
29.	*Periconia* sp.	*Piper longum*	Piperine **(87)**	Compound **(87)** inhibits *M. tuberculosis* and *M. smegmetis* with MIC of 1.74 and 2.62 µg/ml respectively	Verma et al., 2011
30.	*Aschersonia tubulata* BCC 1785	Insect pathogenic fungus	Dustanin **(88)**, 3 beta-acetoxy-15 alpha, 22-dihydroxyhopane **(89)**	Compounds **(88)**, and **(89)**, exhibited anti-mycobacterial activity with the MIC of 12.5 µg/ml	Boonphong et al., 2001
31.	*Aspergillus* sp.		Physcion **(90)**	Compound **(90)** exhibited mycobacterial detoxification enzyme mycothiol-S-conjugate amidase (MAC), with IC_{50} value of 50 µM against *M. smegmatis*	Nicholas et al., 2003
32.	Lichen		Usnic acid **(91)**	Compound **(91)** *M. tuberculosis* (MIC 2.5–5 µg/mL)	Ingólfsdóttir, 2002
33.	*Menisporopsis theobromae*	Seed fungus	Menisporopsin A **(92)**	Compound **(92)** MIC of 50 µg/ml against *M. tuberculosis* H37Ra	Chinworrungsee et al., 2004
34.	fungal strain WZ-4-11 of *Aspergillus carbonarius*		8′-*O*-Demethylnigerone **(93)** and 8′-*O*-demethylisonigerone **(94)**	Compounds **(93)** and **(94)** inhibits *M. tuberculosis* H37Rv with MIC values of 43.0 and 21.5 µM, respectively	Zhang et al., 2008
35.	*Cordyceps* sp. BCC 1861	Insect pathogenic fungus from *Homoptera cicada* nymph	Cordyol A **(95)**	Compound **(95)** showed anti-mycobacterial with a MIC value of 100 µg/mL	Bunyapaiboonsri et al., 2007
36.	*Ophiocordyceps communis* BCC 16475	Insect pathogenic Fungus	Cordycommunin **(96)**	Cordycommunin **(96)** inhibits *M. tuberculosis* H37Ra with an MIC value of 15 µM	Haritakun et al., 2010

Table 1. contd....

Table 1. contd....

Sr. No.	Fungus	Source	Compounds Isolated	Biological Activity*	Reference
37.	*Emericella variecolor*	Marine-derived fungus	Ophiobolin K **(97)**, 6-epi-ophiobolin K **(98)** and 6-epi-ophiobolin G **(99)**	Ophiobolins **(97–99)** inhibited biofilm formation of *M. smegmatis* with MICs of 4.1–65 mM	Arai et al., 2013
				Ophiobolin K **(97)** was also effective against the biofilm formation of *M. bovis* BCG and was able to restore the antimicrobial activity of isoniazid against *M. smegmatis* by inhibiting biofilm formation	
38.	*Emericella rugulosa*		Bicyclo[3.3.1]nona-2,6-diene derivative, rugulosone **(100)**	Compound **(100)**, anti-mycobacterial active	Moosophon et al., 2009
39.	*Conoideocrella tenuis* BCC 18627	Insect pathogenic fungus	Hopan-27-al-6β,11r,22-triol **(101)**, Hopane-6β,11r,22,27-tetraol **(102)**, Hopane-6β,7β,22-triol **(103)**, (atropisomer of ES-242-2) **(104)**, Compound **(105)**	Compounds **(101–105)** active against *M. tuberculosis* H37Ra with MIC of > 105, 52, > 107, > 75, > 75 µM/ml, respectively	Isaka et al., 2011
40.	*Scleroderma citrinum*	Thai mushroom	4,4′-dimethoxyvulpinic acid **(106)**, dibromo derivative of **(106)** 3,3′-dibromo-4,4′-dimethoxyvulpinic acid **(107)** acetyl 4,4′-dimethoxyvulpinate **(108)**	Compounds **(106–108)** inhibits *M. tuberculosis* H37Ra with MIC of 25, 100 and 100 µg/ml	Kanokmedhakul et al., 2003
41.	*Astraeus pteridis*	Truffle-mimiking mushroom	3-epi-astrahygrol **(109)**, astrahygrone **(110)** and 3-epi-astrapteridiol **(111)**	Compounds **(109–111)** inhibits *M. tuberculosis* with MIC values of 58.0, 64.0 and 34.0 µg/mL, respectively	Stanikunaite et al., 2008

42.	*Astraeus odoratus*	Edible mushroom	Astraodoric acids A **(112)** and B **(113)**	Compounds **(112-113)** inhibits *M. tuberculosis* H37Ra with MICs of 50 and 25 µg/mL	Arpha et al., 2012
43.	*Kionochaeta ramifera* BCC 7585	The coral mushroom	Ramiferin **(114)**	Compound **(114)** anti-tubercular MIC 12.7 µM	Bunyapaiboonsri et al., 2008
44.	*Ramaria cystidiophora*	The coral mushroom	Ramariolide **(115)**	Compound **(115)** *M. smegmatis* and *M. tuberculosis* active	Centko et al., 2012
45.	*Mycena* sp. (F205435)	Basidiomycetes	Gliotoxin **(116)**, and S,S dimethyl gliotoxin **(117)**	Compounds **(116-117)** exhibit mycobacterial detoxification enzyme mycothiol-S-conjugate amidase (MAC), with IC_{50} values of 50 and 70 µM against *M. tuberculosis*. Gliotoxin inhibits MAC. Its IC_{50} value is 50 µM against *M. smegmatis*	Nicholas et al., 2003
46.	*Ganoderma orbiforme* BCC 22324	Reishi mushroom	Ganoderic acid T **(118)**, and the C-3 epimer of Ganoderic acid T **(119)**	Compounds **(118-119)**, *M. tuberculosis* H37Ra with MIC of 10.0 and 1.3 µM respectively	Isaka et al., 2013
47.	Endophytic fungi PSU-N24	*Garcinia nigrolineata*	9α-Hydroxyhalorosellinia A **(120)**	Compound **(120)** inhibits *M. tuberculosis* with the MIC value of 12.50 µg/ml	Sommart et al., 2008
48.	Nonsporulating filamentous fungus, F7524		Agonodepside A **(121)** and B **(122)**	Inhibit the 2-trans-enoyl-acyl-reductase involved in mycolic acid biosynthesis. Agonodepside A **(121)** has IC_{50} value of 75 µM, B **(122)** is not active at 100 µM	Cao et al., 2002
49.	*Mortierella alpina* FKI-4905		Calpinactam **(123)**	Calpinactam **(123)** inhibits *M. smegmatis* and *M. tuberculosis* with MICs of 0.78 and 12.5 µg/ml, respectively	Koyama et al., 2010

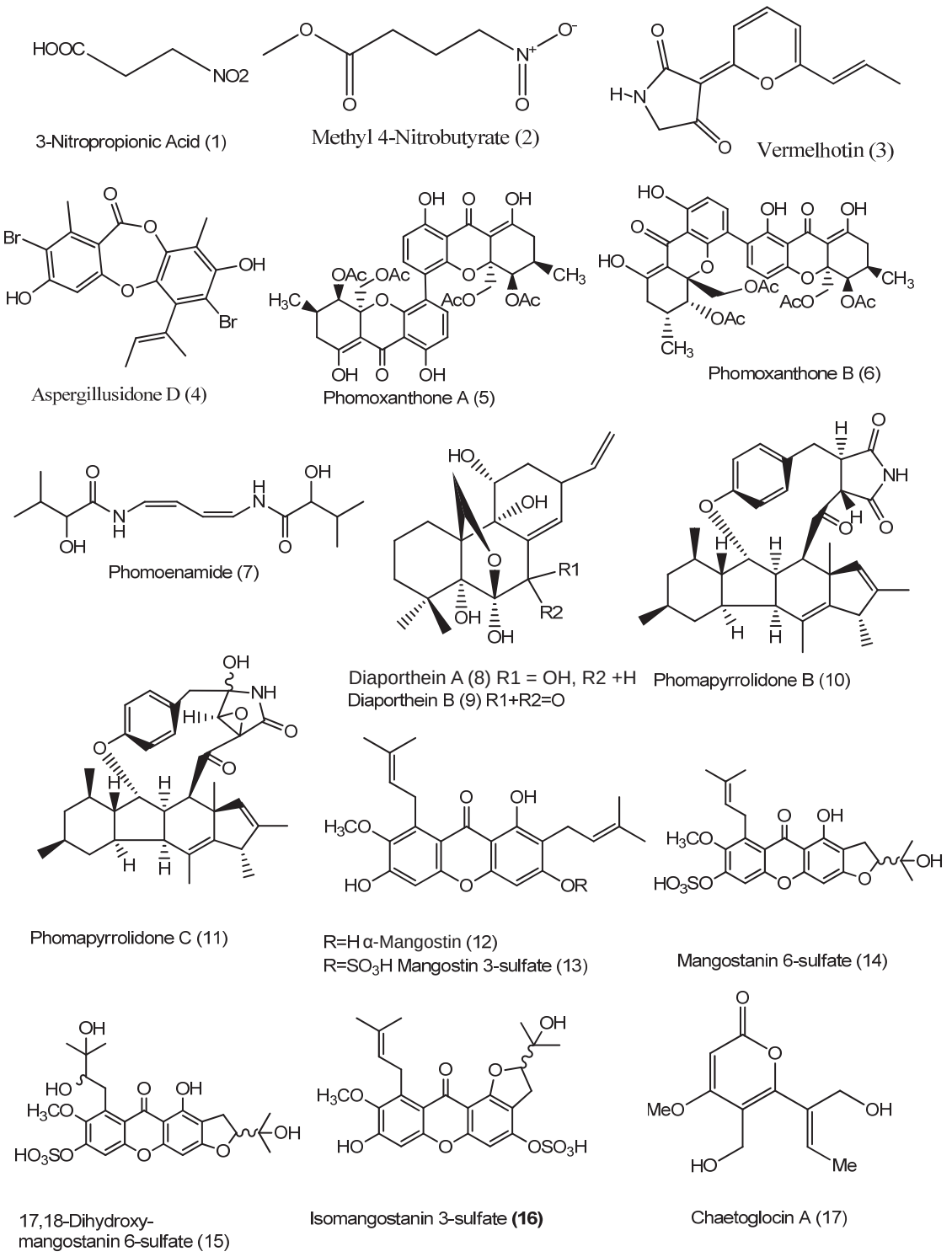


Figure 1. Structures of antimycobacterial metabolites isolated from Ascomycetes **(1-17)**.

for endophytic fungi (Chomcheon et al., 2005). 3-NPA inhibits Isocitrate Lyase (ICL), the enzyme involved in fatty acid catabolism and virulence in *M. tuberculosis* (Munoz-Elias et al., 2005). 3-NPA has MIC values of 12.5 and 50.0 µg/mL against the MTB H37Rv and H37Ra strains, respectively. Out of three derivatives of 3-Nitropropionic acid, Methyl 4-Nitrobutyrate **(2)** is active

with MIC values of 12.5 and 25.0 µg/mL against H37Ra and H37Rv strains, respectively (Ganihigama et al., 2015).

Vermelhotin **(3)** and Aspergillusidone D **(4)** (Fig. 1), were isolated from the marine derived fungus, a *Nodulisporium* sp. (Kasettrathat et al., 2008). Vermelhotin **(3)** is active against five reference strains of *M. tuberculosis* with MICs of 3.1–6.2 µg/mL. Aspergillusidone D **(4)** has an MIC value of 50.0 µg/mL in comparative assays (Ganihigama et al., 2015).

Phomoxanthone A **(5)** and B **(6)** (Fig. 1) were obtained from *Phomopsis* sp. BCC 1323, collected from the leaves of *Tectonagrandis* from the Mee Rim district of Chaingmai Province, Northern Thailand. These compounds show moderate *in vitro* activities with MICs of 0.5 and 6.25 µg/mL, respectively against *M. tuberculosis* H37Ra strain, as compared to Isoniazid and Kanamycin sulphate (MICs of 0.050 and 2.5 µg/mL, respectively) (Isaka et al., 2001). Phomoenamide **(7)** isolated from the endophyte *Phomopsis* sp. PSU-D15 of *Garcinia dulcis* has an MIC of 6.25 µg/mL against *M. tuberculosis* (Rukachaisirikul et al., 2008).

The pimaranediterpenes Diaporthein A **(8)** and B **(9)** (Fig. 1), were isolated from *Diaporthe* sp. BCC 6140. Diaporthein B strongly inhibits *M. tuberculosis* with a MIC 3.1 µg/mL, while A is less active (MIC 200 µg/mL). As compared to Isoniazid, MIC 0.04–0.09 µg/mL and Kanamycin sulfate, MIC of 2.0–5.0 µg/mL (Dettrakul et al., 2003). The results suggest that the carbonyl function C-7 of Diaporthein B is essential for its anti-TB activity (Asres et al., 2001).

Phomapyrrolidone B-C **(10-11)** (Fig. 1), were isolated from the endophyte *Phoma* sp. NRRL 46751, of the plant *Saurauiasca berrinae*. Phomapyrrolidone B **(10)** and C **(11)** have weak *in vitro* anti-tubercular activities when tested in the microplate Alamar Blue assay (MABA) for replicating cultures with MICs of 5.9 and 5.2 µg/ml, respectively and the low oxygen recovery assay (LORA) with MICs of 15.4 and 13.4 µg/ml, respectively for non-replicating *M. tuberculosis* H37Pv (Wijeratne et al., 2013).

α-Mangostin **(12)** (Fig. 1), a prenylatedxanthone from the fruit hull of *Garcinia mangostana*, was individually metabolized by two fungi, *Colletotrichum gloeosporioides* (EYL131) and *Neosartorya spathulata* (EYR042), respectively. Incubation of compound **(12)** with *C. gloeosporioides* (EYL131) gave four metabolites identified as Mangostin 3-sulfate **(13)**, Mangostanin 6-sulfate **(14)**, 17,18-Dihydroxymangostanin 6-sulfate **(15)** and Isomangostanin 3-sulfate **(16)** (Fig. 1). Compound **(13)** was also formed by incubation with *N. spathulata* (EYR042). Compounds **(12)** and **(13)** are active against *M. tuberculosis* (MICs 15.24 and 6.75 µM for 12 and 13, respectively). In contrast, **14–16** showed very week activity (MIC > 50 µg/mL) (Arunrattiyakorn et al., 2011).

Chaetoglocin A **(17)** (Fig. 1) Chaetoglocin B **(18)** (Fig. 2) isolated from *Chaetomium globosum* strain IFB-E036, an endophyte of *Cynodon dactylon* are active against *B. subtilis*, *Streptococcus pyogenes*, *Micrococcus luteus* and *M. smegmatis* with MICs between 8 and 32 µg/mL (Ge et al., 2011). Echinuline **(19)** and Chaetomanone **(20)** (Fig. 2) were isolated from *Chaetomium globosum* KMITL-N0802 isolated from a Thai soil. Chaetomanone and Echinuline have week activities against *M. tuberculosis* with MICs of 169.92 and 216.62

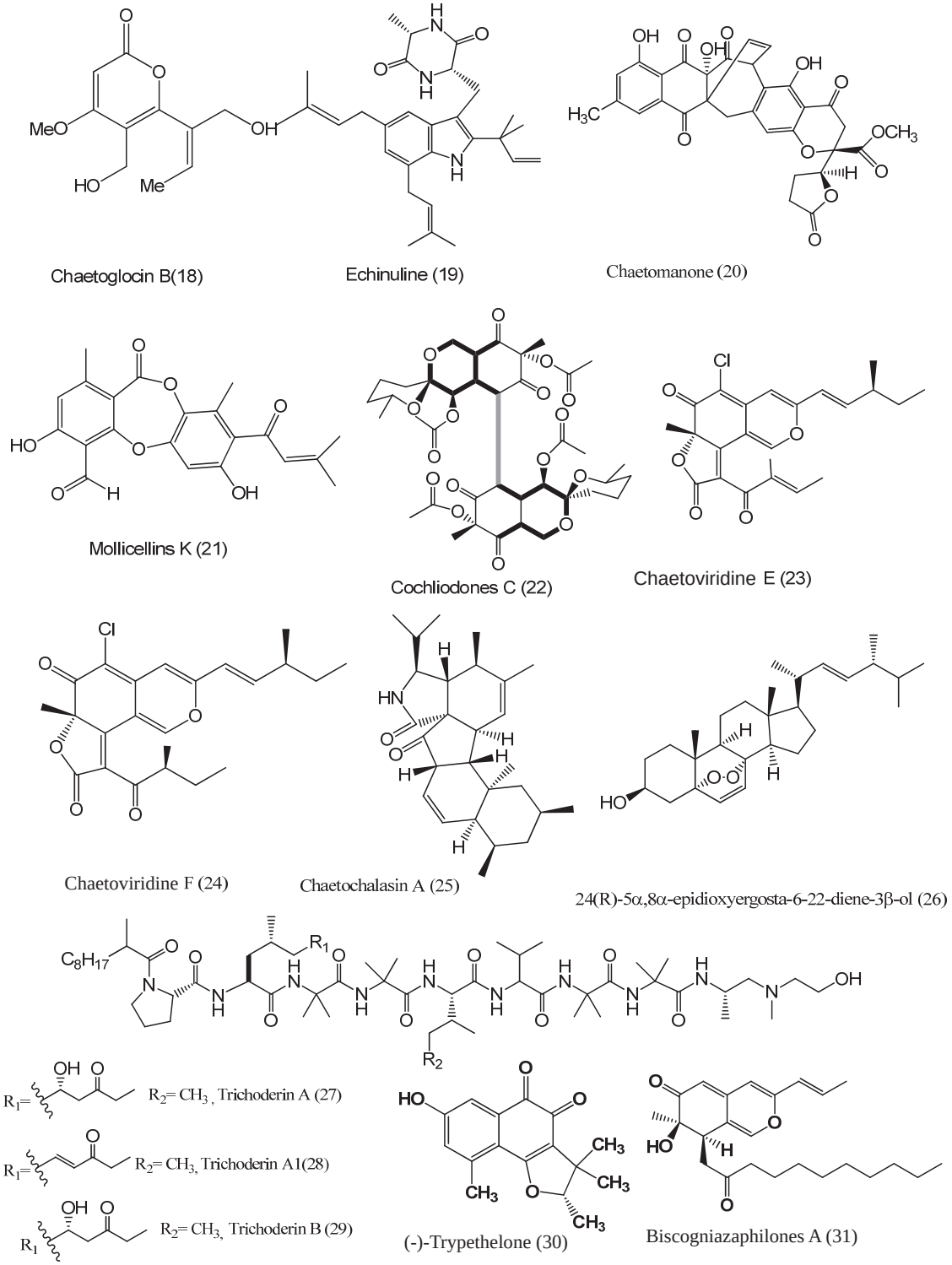


Figure 2. Structures of antimycobacterial metabolites isolated from Ascomycetes **(18-31)**.

µM, respectively (Kanokmedhakul et al., 2002). Mollicellin K **(21)** (Fig. 2) was isolated from the fungus *Chaetomium brasiliense* showed activity against *M. tuberculosis* (MIC 12.5 µg/ml) (Khumkomkhet et al., 2009).

Cochliodone C **(22)**, Chaetoviridine E and F **(23-24)**, Chaetochalasin A **(25)**, 24(R)-5α,8α-epidioxyergosta-6-22-diene-3β-ol **(26)** (Fig. 2) were isolated from

the fungi *Chaetomium cochliodes* VTh01 and *C. cochliodes* CTh05. Compounds **(22–26)** are active against *M. tuberculosis* with MIC values of 200, 50, 100, 100, and 200 µg/mL, respectively (Phonkerd et al., 2008).

Trichoderins A **(27)**, A1 **(28)**, and B **(29)** (Fig. 2), aminolipopeptides from a *Trichoderma* sp., a marine sponge-derived fungus, are reported to be active against both dormant and multiplying *M. tuberculosis* strain H37Rv. Trichoderins are highly active against *M. smegmatis*, *M. bovis* BCG, and *M. tuberculosis* H37Rv with MIC values in the range of 0.02–2.0 µg/mL (Pruksakorn et al., 2010).

(–)-Trypethelone **(30)** (Fig. 2), isolated from the endophyte *Coniothyrium cereale* of the marine green alga *Enteromorpha* sp. is active against *M. phlei*, *S. aureus*, and *E. coli*, at 20 µg/disk/6 mm with inhibition zones of 18, 14, and 12 mm, respectively (Elsebai et al., 2011).

Biscogniazaphilone A **(31)** (Fig. 2) and B **(32)**, N-trans-feruloy-3-O-methyldopamine **(33)**, 5-Hydroxy-3,7,4-trimethoxyflavone **(34)**, 4-Methoxycinnamaldehyde **(35)**, Methyl 3,4-methylenedioxycinnamate **(36)**, 4-Methoxy-trans-cinnamic acid **(37)** (Fig. 3), were all isolated from the endophyte *Biscogniauxia formosana* BCRC 33718, of a *Cinnamomum* sp. Compounds **(31)** and **(32)** are active against *M. tuberculosis* strain H37Rv *in vitro* with MIC values of ≤ 5.12 and ≤ 2.52 µg/mL, respectively, as compared to the clinical drug Ethambutol (MIC 6.25 µg/mL). Compounds **(33–37)** have either moderate or weak anti-mycobacterial activities, MICs of 12.5, 25.0, 42.1, 58.2 and 50.0 µg/mL, respectively (Cheng et al., 2012).

Javanicin **(38)**, 3-O-methylfusarubin **(39)**, a diastereomer of Dihydronaphthalenone **(40)** and 5-Hydroxy-3-methoxydihydrofusarubin A **(41)** (Fig. 3) were isolated from the endophyte, a *Fusarium* sp. BCC 14842 of the Bamboo leaf, collected from a forest of Nam Nao National Park, Phetchabun Province, Thailand. Compounds **(38)** and **(40)**, have moderate activities (MICs of 25 µg/mL), while 3-O-methylfusarubin **(39)**, and 5-hydroxy-3-methoxydihydrofusarubin A **(41)**, have weak antimycobacterial activities (MICs of 50 µg/mL) (Kornsakulkarn et al., 2011).

Fusaric acid was isolated from a *Fusarium* sp., an endophyte of a mangrove plant. Cadmium and Copper complexes were prepared. The Cadmium **(42)** and Copper **(43)** (Fig. 3), complexes showed potent activities against *M. bovis* BCG (MIC 4 µg/mL) and *M. tuberculosis* H37Rv (MIC 10 µg/mL) (Pan et al., 2011).

9α-Hydroxyhalorosellinia A **(44)**, Nigrosporin **(45)** Anhydrofusarubin **(46)** (Fig. 3), were isolated from the sea fan-derived fungi *Fusarium* spp. PSU-F14. Compounds **(44–46)** were found active against *M. tuberculosis* H37Ra, with MICs of 39, 41 and 87 µM, respectively (Trisuwan et al., 2010).

3′-O-Demethylpreussomerin I **(47)**, Preussomerin E **(48)**, (Fig. 3), Preussomerins F–I **(49–52)** (Fig. 4), Deoxypreussomerin A **(53)** (Fig. 4) and Bipendensin (Palmarumycin C11) **(54)** (Fig. 4), were isolated from *Microsphaeropsis* sp. BCC 3050, a lichenicolous fungus of *Dirinaria applanata* collected from Phu Tee-Suan-Sai forest in Loei province, Northeastern

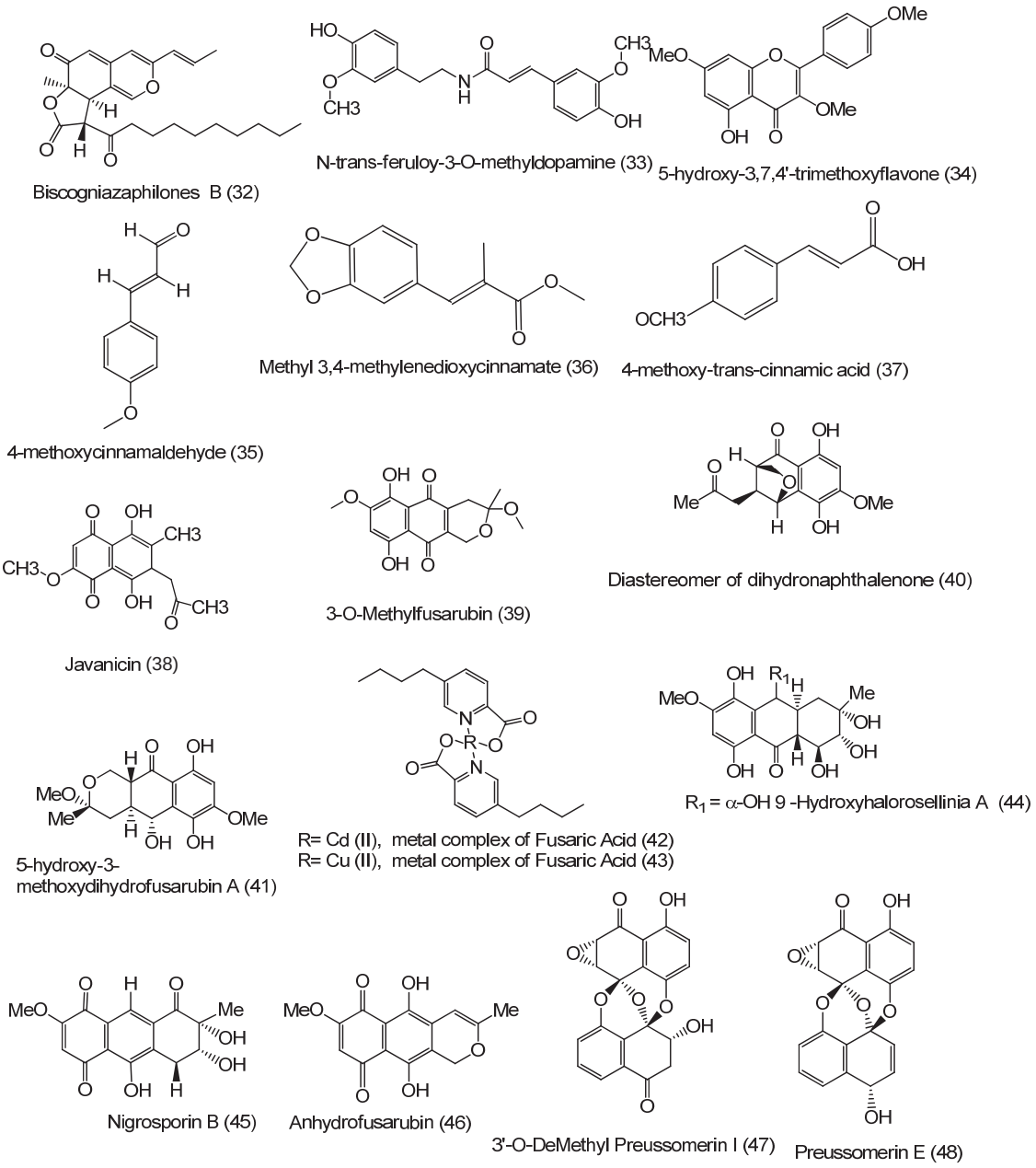
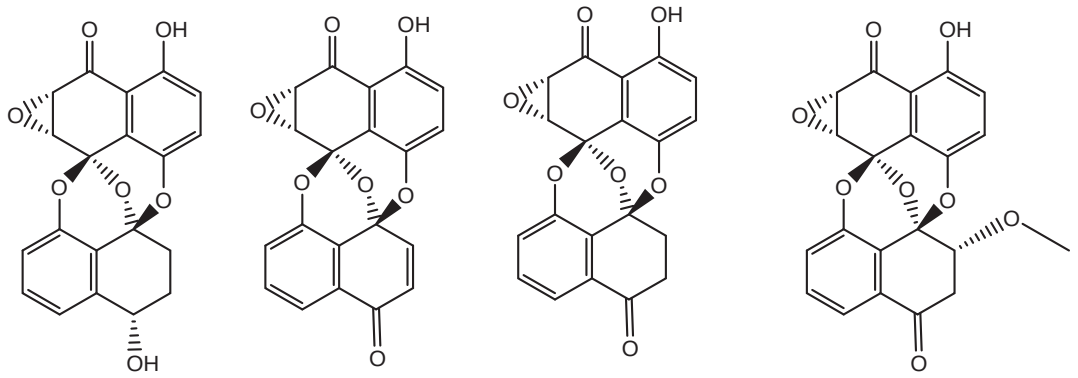


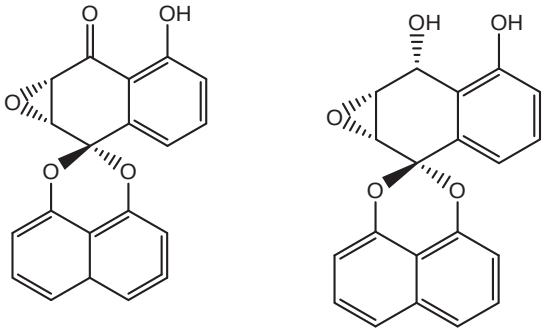
Figure 3. Structures of antimycobacterial metabolites isolated from Ascomycetes **(32-48)**.

Thailand. These compounds **(47–54)** are active against *M. tuberculosis* H37Ra (MICs 25, 3.12, 3.12–6.25, 6.25, 12.5, 25, 1.56–3.12, 50 µg/mL, respectively) (Seephonkai et al., 2002).

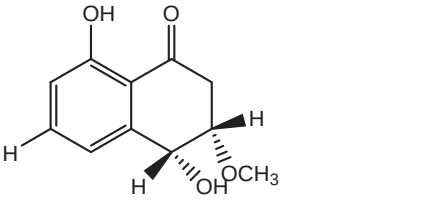
(3S,4 R)-4,8-Dihydroxy-3-methoxy-3,4-dihydro-1(2 H)-naphthalenone **(55)**, (S)-4,6,8-Trihydroxy-3,4-dihydro-1(2H)-naphthalenone **(56)**, (3S,4S)-3,4,8-Trihydroxy-6-methoxy-3,4-dihydro-1(2 H)-naphthalenone **(57)**, 6-Ethyl-5-hydroxy-2,7-dimethoxynaphthoquinone **(58)**, 6-(1-Acetoxyethyl)-5-hydroxy-2,7-dimethoxynaphthoquinone **(59)**, Deacetylkirschsteinin **(60)** (Fig. 4) were isolated from a *Phaeosphaeria* sp. Compounds **(55)** and **(56)** have good anti-mycobacterial activity with MICs of 12.50 µg/mL. Compound **(58)**



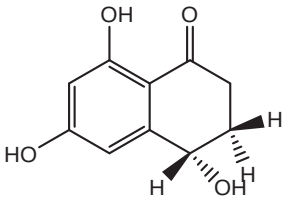
Preussomerin F (49) Preussomerin G (50) Preussomerin H (51) Preussomerin I (52)



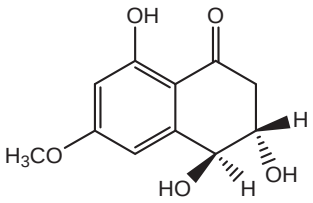
Deoxypreussomerin A (53) Bipendensin (Palmarumycin C11) (54)



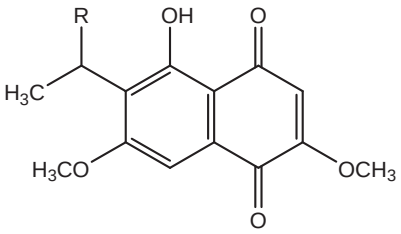
(3S,4 R)-4,8-Dihydroxy-3-methoxy-3,4-dihydro-1(2 H)-naphthalenone (55)



(S)-4,6,8-Trihydroxy-3,4-dihydro-1(2H)-naphthalenone (56)

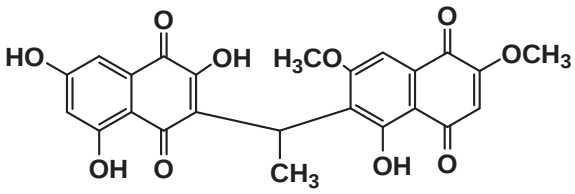


(3S,4S)-3,4,8-Trihydroxy -6-methoxy -3,4-dihydro-1(2 H) -naphthalenone (57)



R=H ; 6-Ethyl-5-hydroxy-2,7-dimethoxynaphthoquinone (58)

R= OCOCH3; 6-(1-Acetoxyethyl) -5-hydroxy-2,7-dimethoxynaphthoquinone (59)



Deacetylkirschsteinin (60)

Figure 4. Structures of antimycobacterials metabolites isolated from Ascomycetes **(49-60)**.

exhibited anti-TB activity with MIC of 12.50 µg/mL, while its acetyl derivative, compound **(59)**, has excellent anti-TB activity, MIC 0.39 µg/mL. Compound **(60)** has an MIC value of 6.25 µg/mL, while compound **(57)** has an MIC of 25 µg/mL as compared to MIC values of isoniazid and kanamycin sulphate that were 0.05 and 2.5 µg/mL, respectively (Pittayakhajonwut et al., 2008).

2-hydroxymethyl-3-methylcyclopent-2-enone **(61)**, Asterric acid **(62)** and hydrazone derivative of cis-2-hydroxymethyl-3-methylcyclopentanone **(63)** (Fig. 4), were all isolated from a *Dothideomycete* sp. LRUB20, an endophyte of the stem of a medicinal plant *Leearubra* in Thai. Compounds **(61-63)** have low anti-mycobacterial activities with MIC values of 200 µg/mL (Chomcheon et al., 2006).

Peniphenone B **(64)** and C **(65)** (Fig. 5), were isolated from *Penicillium dipodomyicola* - HN4-3A of the stem of the mangrove plant *Acanthusilicifolius* collected from the South China Sea in Hainan Province, China. Both B and C exhibited strong inhibitory activity against protein tyrosine phosphatase B (MptpB) with IC50 values of 0.16 ± 0.02 and 1.37 ± 0.05 µM, respectively (Li et al., 2014).

7-butyl-6,8-dihydroxy-3(R)-pent-11-enylisochroman-1-one **(66)**, 7-but-15-enyl-6,8-dihydroxy-3(R)-pent-11-enylisochroman-1-one **(67)** and 7-butyl-6,8-dihydroxy-3(R)-pentylisochroman-1-one **(68)** (Fig. 5) novel Dihydroisocoumarins were isolated from a *Geotrichum* sp., an endophyte of *Crassocephalum crepidoides*. The MICs of compounds **(66–68)** were, 25 µg/mL, 50 µg/mL, and inactive against *M. tuberculosis* H37Ra respectively. This suggests that the double bond C11-C12 and the aliphatic group at C14-C17 are important for the biological activities (Kongsaeree et al., 2003).

Four cyclic peptides, namely, Enniatins B **(69)**, B4 **(70)**, G **(71)**, C **(72)** (Fig. 5) were isolated from a pathogenic fungus *Verticillium hemipterigenum.* Analogues H **(73)**, I **(74)** and MK1688 **(75)** (Fig. 5), were prepared by feeding the substrate analogs L-leucine and L-isoleucine to the fermentation. Compounds **(69–75)**, inhibited *M. tuberculosis* H37Ra (MIC 3.12, 3.12, 6.25, 6.25, 6.25, 6.25 and 1.56 µg/mL, respectively) (Nilanonta et al., 2003). Fermentation of an unidentified Thai fungus led to the isolation of new hydroxyl analogs Enniatins L **(76)**, M1 **(77)**, M2 **(78)** and N **(79)** (Fig. 5) with MICs of 6.25–12.5 µg/ml (Vongvilai et al., 2004).

4-Deoxybostrycin **(80)** (Fig. 5) and Nigrosporin **(45)** (Fig. 3) were isolated from the mangrove endophyte, a *Nigrospora* sp. collected from the South China Sea. In the Kirby-Bauer disk diffusion susceptibility test, both showed zones of over 25 mm against *M. tuberculosis*. Compound **(80)** has activity against multidrug-resistant (MDR) *M. tuberculosis* strains with MICs of < 5–39.0 µg/ml. The gene expression profile of *M. tuberculosis* H37Rv after treatment with 4-Deoxybostrycin was compared with that of the untreated bacteria. One hundred and nineteen out of 3,875 genes were significantly different in *M. tuberculosis* exposed to 4-deoxybostrycin from that of the control. There are 46 functionally known genes involved in metabolism, information storage and processing, and cellular processes. The differential expressions of six

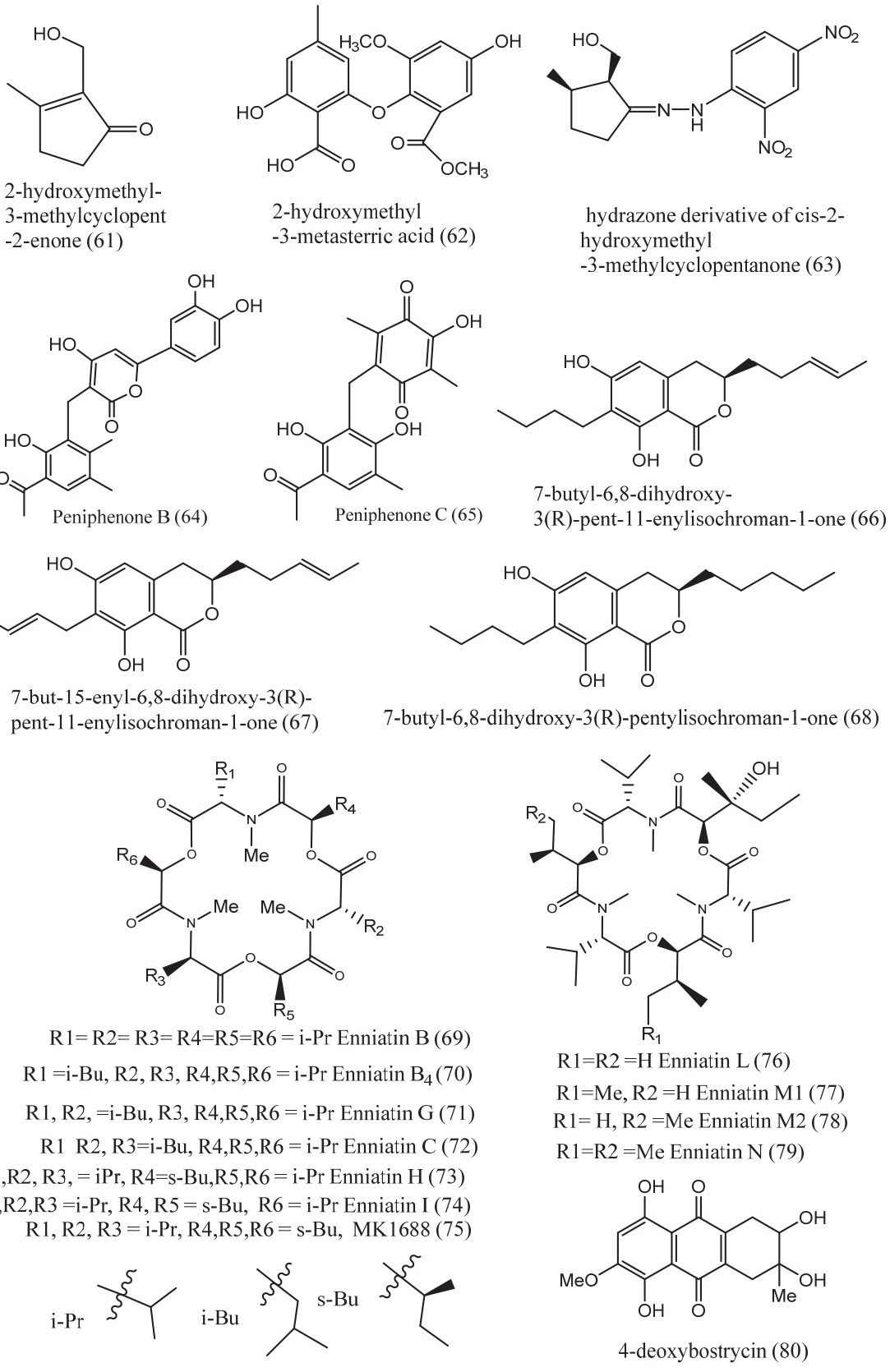


Figure 5. Structures of antimycobacterial metabolites isolated from Ascomycetes **(61-80)**.

genes were confirmed by quantitative real-time polymerase chain reaction (qRT-PCR) (Wang et al., 2013).

Hirsutellide A **(81)** (Fig. 6), was isolated from the entomopathogenic fungus *Hirsutella kobayasii* BCC 1660. It was active against *M. tuberculosis* H37Ra in

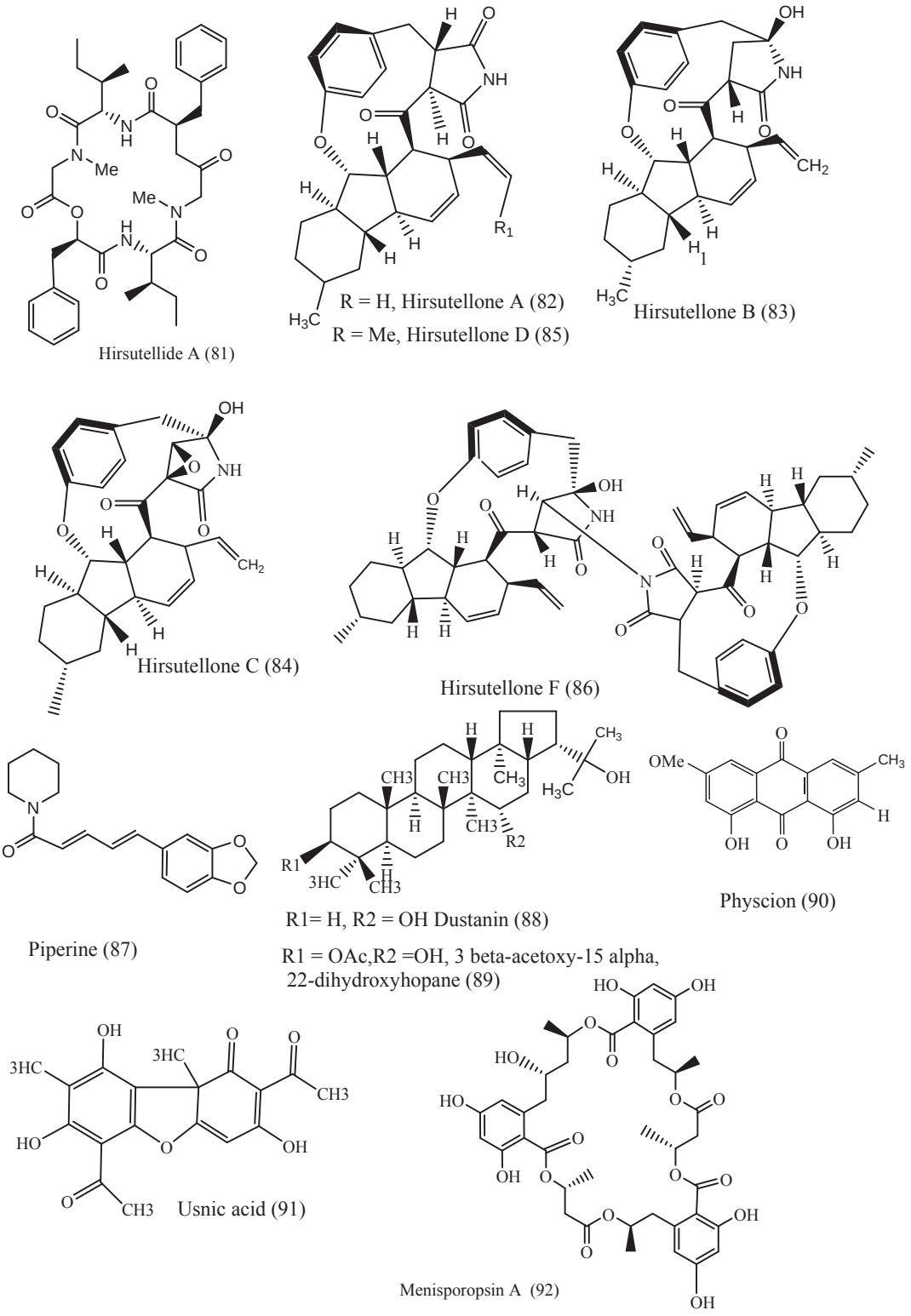


Figure 6. Structures of antimycobacterial metabolites isolated from Ascomycetes **(81-92)**.

Microplate Alamar Blue Assay (MABA) with an MIC with 6–12 µg/mL and no cytotoxicity against Vero cells at 50 µg/mL (Vongvanich et al., 2002).

Hirsutellones A–D **(82–85)** (Fig. 6), of the pathogenic fungus *Hirsutella nivea* BCC 2594 from Thailand, inhibited *M. tuberculosis* H37Ra (MIC 0.78, 3.125, 0.78, 0.78 µg/mL, respectively) (Isaka et al., 2005). Hirsutellone F **(86)** (Fig. 6), a new dimer alkaloid along with the known Hirsutellones A, B, and C, from the spores of the fungus *Trichoderma* sp. BCC 7579 showed a weaker activity against *M. tuberculosis* H37Ra (MIC 3.12 µg/mL) than the Hirsutellones A, B, and C (Isaka et al., 2006).

Piperine **(87)** (Fig. 5), is obtained from an endophytic *Periconia* sp. of *Piper longum*. Piperine has very good anti-mycobacterial activity against *M. tuberculosis* and *M. smegmetis* with MIC of 1.74 and 2.62 µg/ml, respectively (Verma et al., 2011).

Dustanin **(88)** and 3 beta-acetoxy-15 alpha, 22-dihydroxyhopane **(89)** (Fig. 6), were isolated from the insect pathogenic fungus *Aschersonia tubulata* BCC 1785. Compounds **(88)**, and **(89)**, have anti-mycobacterial activities with MICs of 12.5 µg/ml (Boonphong et al., 2001).

Physcion **(90)** (Fig. 6), isolated from an *Aspergillus* sp. inhibited the mycobacterial detoxification enzyme, mycothiol-S-conjugate amidase (MAC) with IC_{50} of 50 µM against *M. smegmatis* (Nicholas et al., 2003). The dibenzofuran derivative, Usnic acid **(91)** (Fig. 6), a secondary metabolite of lichen, inhibits *M. tuberculosis*, MIC 2.5–5 µg/mL (König and Wright, 1999; Ingólfsdóttir, 2002).

A phenolic macrocyclicpolylactone, Menisporopsin A **(92)** (Fig. 6), reported from the seed fungus *Menisporopsis theobromae* has weak activity with MIC of 50 µg/ml against *M. tuberculosis* H37Ra (Chinworrungsee et al., 2004).

8′-*O*-Demethylnigerone **(93)** and 8′-*O*-Demethylisonigerone **(94)** (Fig. 7), dimericnaphtho-gamma-pyrones, were isolated from strain WZ-4-11 of *Aspergillus carbonarius*. Compounds **(93)** and **(94)** have weak activities against *M. tuberculosis* H37Rv (MICs of 43.0 and 21.5 µM, respectively) (Zhang et al., 2008).

Cordyol A **(95)** (Fig. 7), was isolated from *Cordyceps* sp. BCC 1861 of *Homoptera cicada* nymph of the KhaoLaem National Park, Kanchanaburi Province, Thailand. Cordyol A has weak anti-mycobacterial activity with MIC 100 µg/mL (Bunyapaiboonsri et al., 2007).

A novel cyclodepsipeptide, Cordycommunin **(96)** (Fig. 7), isolated from the insect pathogenic fungus *Ophiocordyceps communis* BCC 16475 inhibits *M. tuberculosis* H37Ra, MIC 15 µM. This compound has weak cytotoxic effect on KB cell line with an IC_{50} of 45 µM but inactive against BC, NCI-H187 and Vero cell lines at 88 µM (50 µg/mL) (Haritakun et al., 2010).

Ophiobolin K **(97)**, 6-epi-ophiobolin K **(98)** and 6-epi-ophiobolin G **(99)** (Fig. 7), were isolated from the marine-derived fungus *Emericella variecolor*. Ophiobolins **(97–99)** inhibited biofilm formation of *M. smegmatis* at MICs of 4.1–65 mM, whereas these compounds do not show anti-microbial activity at the concentrations that show anti-biofilm formation. Ophiobolin K **(97)** is

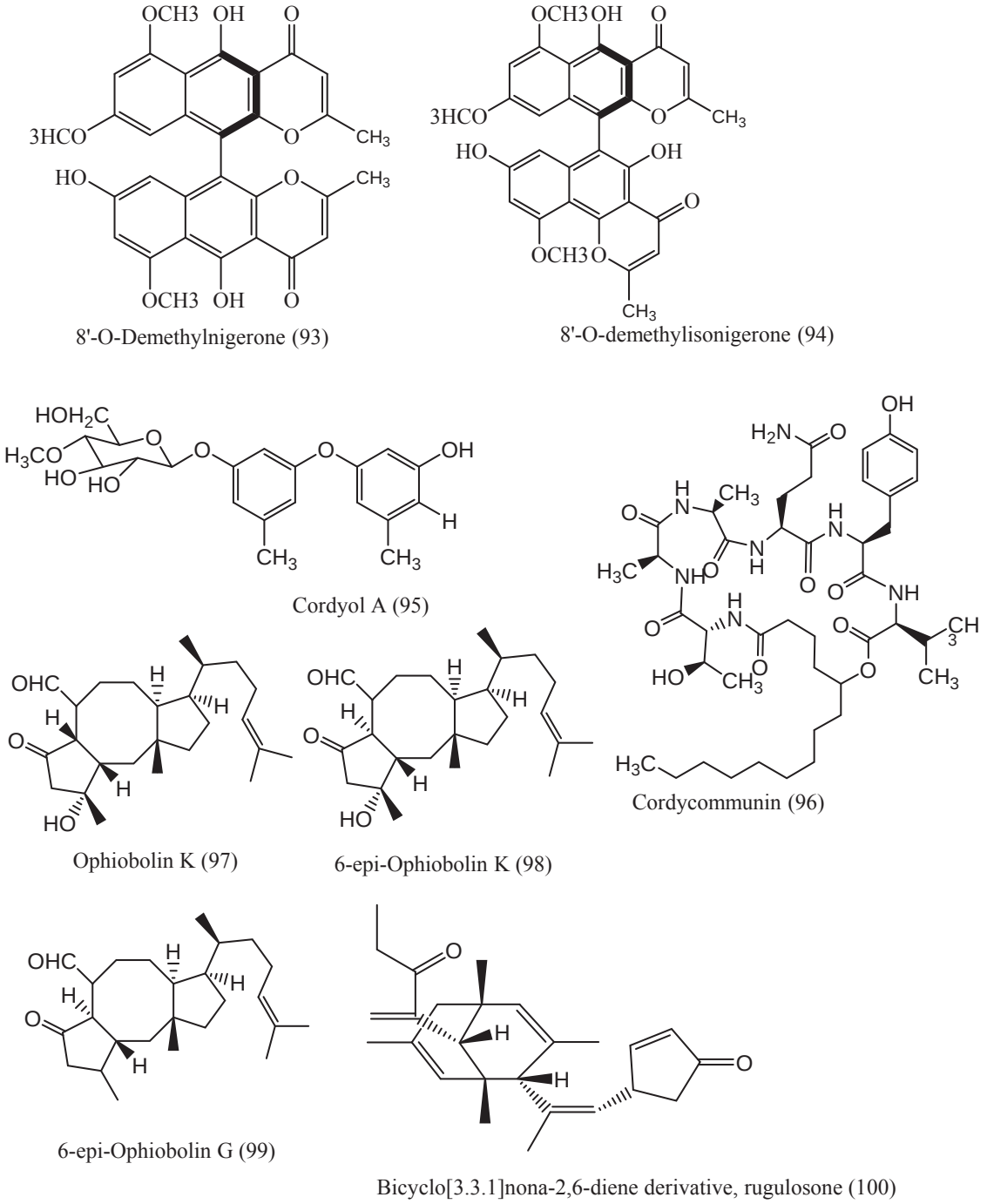
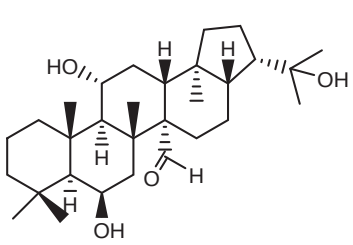


Figure 7. Structures of antimycobacterial metabolites isolated from Ascomycetes **(93-100)**.

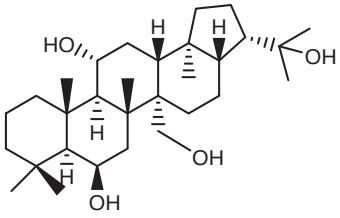
also effective against the biofilm formation of *M. bovis* BCG and is thus able to restore the anti-microbial activity of isoniazid against *M. smegmatis* (Arai et al., 2013).

The Bicyclo[3.3.1]nona-2,6-diene derivative, Rugulosone **(100)** (Fig. 7), was isolated from *Emericella rugulosa.* It showed anti-malarial and anti-mycobacterial activities, as well as cytotoxicity against three cancer cell lines (Moosophon et al., 2009).

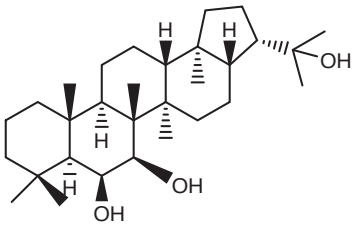
Hopan-27-al-6β,11α,22-triol **(101)**, Hopane-6β,11r,22,27-tetraol **(102)**, Hopane-6β,7β,22-triol **(103)**, Compound **(104)** (atropisomer of ES-242-2) and Compound **(105)** (Fig. 8), were isolated from the scale insect pathogenic fungus *Conoideocrella tenuis* BCC 18627. Compounds **(101–105)** are active against *M. tuberculosis* H37Ra, MIC of > 105, 52, > 107, > 75, > 75 μM/ml, respectively. The MIC values of standard anti-TB drug Isoniazid were 0.17–0.34 μM (Isaka et al., 2011).



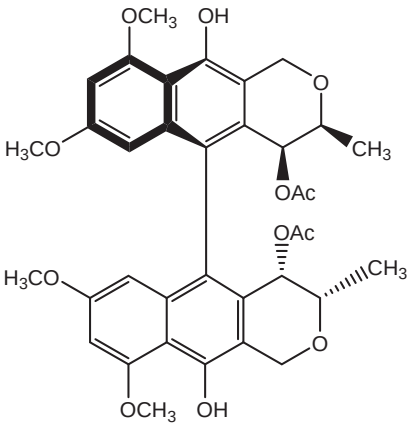
Hopan-27-al-6β,11r,22-triol (101)



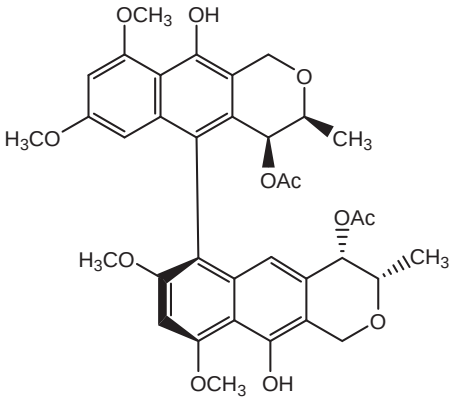
Hopane-6β,11r,22,27-tetraol (102)



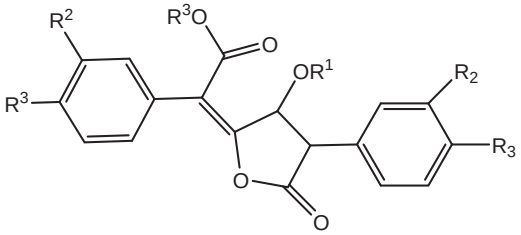
Hopane-6β,7β,22-triol (103)



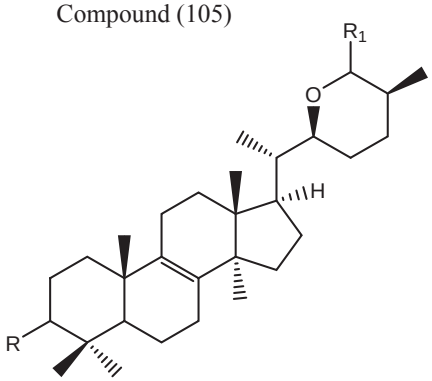
Compound (104) (Atropisomer of ES-242-2)



Compound (105)



R1=R2= H, R3 =Me
4,4'-dimethoxyvulpinic acid (106)
R1= H, R2=Br, R3 =Me
3,3'-dibromo- 4,4'-dimethoxyvulpinic acid (107)
R1= Ac, R2= H, R3 =Me
Acetyl 4,4'-dimethoxyvulpinate (108)



R= α-OH, R1=O 3-epi-astrahygrol (109)
R = R1 =O Astrahygrone (110)
R=R1= α-OH 3-epi-astrapteridiol (111)

Figure 8. Structures of antimycobacterial metabolites isolated from Ascomycetes **(101-105)** and Basidiomycetes **(106-111)**.

From Basidiomycetes

4,4′-dimethoxyvulpinic acid **(106)** (Fig. 8), was isolated from the Thai mushroom *Scleroderma citrinum.* In addition, the dibromo derivative of **(106)** 3,3′-dibromo-4,4′-dimethoxyvulpinic acid **(107)** and the acetate derivative acetyl 4,4′-dimethoxyvulpinate **(108)** were also prepared. All the compounds are active against *M. tuberculosis* H37Ra with MICs 25, 100 and 100 µg/ml, respectively (Kanokmedhakul et al., 2003).

3-Epi-astrahygrol **(109)**, Astrahygrone **(110)** and 3-epi-astrapteridiol **(111)** (Fig. 8), were isolated from, the truffle-mimicking mushroom, *Astraeus pteridis*. Compounds **(111) (109)** and **(110)** showed moderate activity against *M. tuberculosis* with MIC values of 34.0, 58.0, and 64.0 µg/mL, respectively (Stanikunaite et al., 2008).

Lanostanetriterpenes, Astraodoric acids A **(112)** and B **(113)** (Fig. 9), were isolated from, an edible mushroom, *Astraeus odoratus.* Compounds **(112)** and **(113)** exhibited moderate activities against *M. tuberculosis* H_{37}Ra (MICs of 50 and 25 µg/mL) and cytotoxic activities (IC_{50}) values of 34.69 and 18.57 µg/mL against KB cancer cells lines and 19.99 and 48.35 µg/mL against NCI-H187 cancer cells lines, respectively (Arpha et al., 2012).

A new bisphenol-sesquiterpene, Ramiferin **(114)** (Fig. 9), isolated from the fungus *Kionochaeta ramifera* BCC 7585 has anti-tubercular activity, MIC 12.7 µM. It is toxic against three cancer cell lines (BC, KB and NCI-H187) and nonmalignant Vero cells with IC_{50} values of 9.1, 12.6, 13.0, and 9.7 µM, respectively (Bunyapaiboonsri et al., 2008).

Ramariolides A **(115)** (Fig. 9), a Butenolides was isolated from the fruiting bodies of a coral mushroom *Ramaria cystidiophora*. Ramariolide A has an unusual spirooxiranebutenolide moiety and shows *in vitro* activity against *M. smegmatis* and *M. tuberculosis* (Centko et al., 2012).

Gliotoxin **(116)**, and S,S dimethyl gliotoxin **(117)** (Fig. 9), isolated from *Mycena* sp. (F205435) inhibited the mycobacterial detoxification enzyme mycothiol-S-conjugate amidase (MAC) of *M. tuberculosis* with IC_{50} of 50 and 70 µM. Both compounds inhibited MAC of *M. smegmatis* with IC_{50} value of 50 µM each (Nicholas et al., 2003).

Ganoderic acid T **(118)**, and the C-3 epimer of Ganoderic acid T **(119)** (Fig. 9), were isolated from *Ganoderma orbiforme* BCC 22324. Compounds **(118-119)**, are active against *M. tuberculosis* H37Ra with MICs of 10.0 and 1.3 µM, respectively (Isaka et al., 2013).

From Unidentified Fungus

9α-hydroxyhalorosellinia A **(120)** (Fig. 9), was isolated from an endophytic fungus PSU-N24 from *Garcinia nigrolineata*, collected from the Ton Nga Chang wildlife sanctuary, Songkhla province, Southern Thailand. It is active against *M. tuberculosis,* MIC 12.50 µg/ml (Sommart et al., 2008).

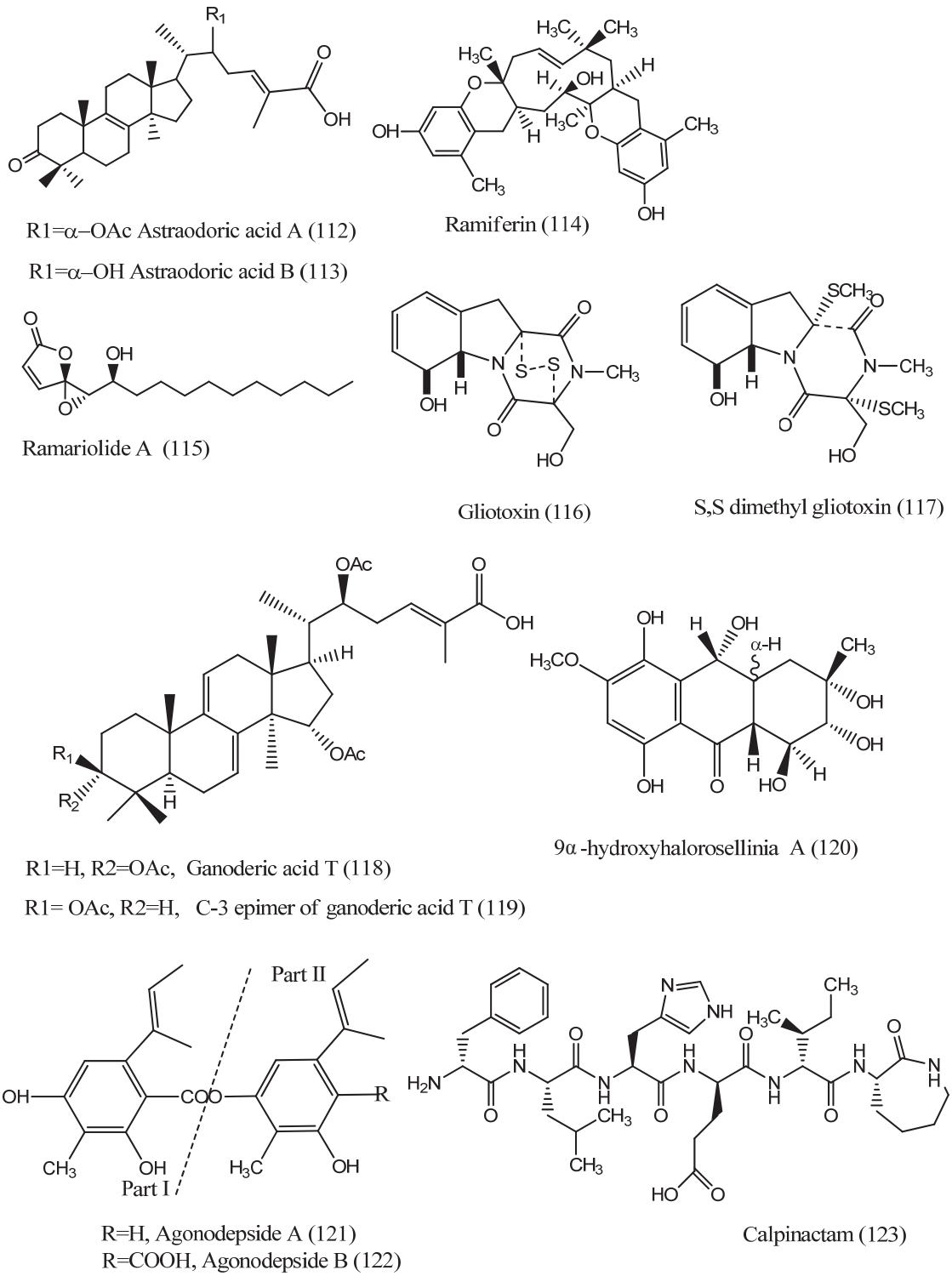


Figure 9. Structures of antimycobacterials metabolites isolated from Basidiomycetes **(107-119)**, Unidentified fungus **(120-122)** and Zygomycetes **(123)**.

Agonodepside A **(121)** and B **(122)** (Fig. 9), were isolated from a non-sporulating filamentous fungus, F7524. They inhibited the mycobacterial InhA enzyme, a 2-trans-enoyl-acyl-reductase involved in Mycolic acid biosynthesis, which is a major lipid of the mycobacterial envelope.

Agonodepside A had moderate activity, with an IC_{50} of 75 µM, while Agonodepside B is not active at 100 µM (Cao et al., 2002).

From Zygomycetes

Calpinactam **(123)** (Fig. 9) was isolated from *Mortierella alpina* FKI-4905. Calpinactam inhibits *M. smegmatis* and *M. tuberculosis* with MIC values of 0.78 and 12.5 µg/ml, respectively (Koyama et al., 2010).

Volatile Organic Compounds (VOCs) as Antimycobacterials

A stain of *Muscodor* namely, *Muscodor crispans* of *Ananas ananassoides* (wild pineapple) growing in the Bolivian Amazon Basin produces VOCs namely, Propanoic acid, 2-methyl-, 1-butanol, 3-methyl-1-butanol, 3-methyl-, acetate propanoic acid, 2-methyl-, 2-methylbutyl ester, and ethanol. The VOCs of this fungus are effective against *Xanthomonas axonopodis* pv. *citri*, a citrus pathogen and also on several human pathogens, including *Yersinia pestis*, *M. tuberculosis* and *Staphylococcus aureus*. *Muscodor crispans* is only effective against the vegetative cells of *Bacillus anthracis* and not against its spores. Artificial mixtures of the fungal VOCs were both inhibitory and lethal to a number of human and plant pathogens, including three drug-resistant strains of *M. tuberculosis* (Mitchell et al., 2010). The mechanism of action of the VOCs of *Muscodor* spp. on target bacteria is unknown. A microarray study of the transcriptional response analysis of *B. subtilis* cells exposed to *M. albus* VOCs show that the expression of genes involved in DNA repair and replication increased, suggesting that VOCs induce some type of DNA damage in cells, possibly through the effect of one of their naphthalene derivatives (Mitchell et al., 2010).

Outlook /Conclusion/Suggestions

In the poorer countries of the world and particularly those of the Asian Subcontinent, *M. tuberculosis* remains a persistent problem with very few solutions in sight. This is of course due to the extreme poverty of the populations in such third world countries. Typically Nepal, Tibet, North Eastern India (such as Assam), where communications are very weak both due to the inaccessibility of many of the remote area and language problem. The extreme poverty leads to very poor nutrition. Inadequate medical facilities, some time totally missing in many parts of North India, Nepal and Tibet exits even today. Distribution of effective of effective medicine is a huge and difficult task. Affordable medicine? Follow up? There is no light of the end of this tunnel of disease!! Unless there is a 'United Front To Combat Tuberculosis' worldwide This front must be supported by a world with consortium of countries such as UN WHO plus the other advanced countries of the world!!

Will it happen? The mindset of the nations of the world should change from "what can we suggest" to a "what can we do" to solve such great a problem!

Do!

Consider the use of complex mixture of Ayurvedic and allopathic compounds, already been used. Variations in regimens of treatment may also be the part such new initiatives.

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ISBN:978-93-84298-56-2

A Microbial Bioremediation Solution to Azo Dye Pollution

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Abstract: The release of highly coloured synthetic dye effluents into inland and coastal waters is an environmental problem of increasing alarm. Of these dyestuffs, azo dyes have long constituted the most prominent threat to the environment. Azo dyes contain one or more azo linkages and make up 70% of the dyestuffs produced. Azo dyes mainly produce aromatic amines on degradation, many of which are carcinogenic. Bioremediation has long played an important role in protecting the environment against such threats. The aim of the current study was therefore to provide a solution to this environmental problem by isolating bacteria that can degrade azo dyes and studying conditions that could optimize this degradation. To this end, water bodies in Mumbai that are subjected to industrial dumping were chosen as a source of microorganisms. Congo red, a well-known azo dye, with cytotoxic properties, was chosen as the target dye against which the dye degrading potential of micro-organisms was studied. Of the various isolates that could degrade the dye, the isolate with the highest potential was chosen for further study and for optimization of the temperature, pH and time required for maximum degradation. The isolate was also studied for its ability to degrade other dyes such as Toluidine Blue, Methyl Red, and Acid Orange and identified on the basis of 16S rRNA gene sequencing. Cytotoxicity of the degraded product was analysed to ensure that the degraded product did not add to the pollution load. Thus an efficient azo dye degrader with a wide spectrum of activity in terms of substrate, temperature and pH was successfully isolated and studied for potential bioremediation use.

INTRODUCTION

Today, more than 100,000 commercial dyes are available in the market and among them more than fifty percent are azo dyes. Azo dyes are the largest class of synthetic dyes having '-N=N-' group in its structure. Moreover, they are cheap and known to produce highest range of colours. These dyes are most popularly used for textile, cosmetic, paper and leather industries and nearly 10% of dyes are released in the environment and natural resources as dyestuff waste. According to literature, dyeing and finishing of one ton of fabric can result in the pollution of up to 200 tons of water.In India, the textile industry contributes nearly 14% of total industrial production and the market demand for dyes are increasing.

The disposal of these coloured substances not only pose major problems in waste water treatment but health issues as they are toxic to aquatic life and even carcinogenic or mutagenic in nature . Azo dyes have long been recognized as human urinary bladder carcinogens, which are also tumorigenic in animals and cyanogenic in fishes. The azo dyes are also known to reduce seed germination rate and induce dwarfism in plants .

Varieties of microorganisms including bacteria, fungi, yeasts, actinomycetes and algae are capable of degrading azo dyes, among which bacterial cells represent an inexpensive and promising tool for the removal of various azo dyes from textile dye effluents . In the current scenario, microbial or enzymatic treatment offers an indispensable, ecofriendly and cost-effective solution towards restoring azo dye polluted ecosystems . Bacteria capable of dye decolorization, either in pure cultures or in consortia, have been reported earlier . The mode of degradation of the azo dyes is by production of azoreductase enzyme which cleaves the azo bond and converts azo compounds to colourless amines and functional groups .

ISBN:978-93-84298-56-2

In the present study, azo dye, Congo red was used for initial enrichment and isolation of the dye degrader and parameter optimization studies. Congo red is an azo dye with a structure 3, 3'-((biphenyl)-4,4'-diylbis(azo))-bis(4- amino-1-naphthalenesulphonicacid), which is a disodium salt. It is intended primarily for the coloration of paper products, for use in medicine (as a biological stain) and as an indicator since it turns from red-brown in basic medium to blue in acidic. It is used widely to color textile and wood pulp. It acts as a potent carcinogen and mutagenic agent because of the presence of aromatic amine group.

The present study deals with the isolation and identification of a bacterial strain from dye contaminated water of textile industry and to evaluate its ability to decolorize azo dye, Congo red under various conditions. The cytotoxicity of the dye degraded product was also analyzed by seed germination and MTT assay.

MATERIALS AND METHODS

Sample collection, Enrichment and Isolation

The sampling site, Nandivli nullah, a part of the Ulhas river (Dombivli, Maharashtra, India) was chosen as it contains effluents of various textile industries. The effluent sample was inoculated in sterile mineral salt media (MSM) with 100 ppm Congo red dye(The British Dye House, England) for initial enrichment .The Flasks were incubated for 24 hours at 37°C on a rotary shaker (170rpm) for 48h. The culture from the enrichment flasks that showed considerable decolourisation were plated (T streak method) onto Nutrient Agar plates containing 100ppm of Congo red dye. Each colony on the plates showing the presence of a colorless patch was picked up by a sterile toothpick and placed in tubes containing nutrient broth along with 100ppm of Congo red which were then incubated at 37°C for 72 hours.

Testing for degradation of Congo red

Pure cultures were tested for their ability to decolorize Congo red by spectrophotometric analysis . Briefly, MSM containing100ppm Congo red media was inoculated with 5% culture (OD=0.1) volume / volume. After 48 hours of incubation,a 1.5 ml aliquot of the decolorized culture broth was placed in Eppendorf tubes and centrifuged at 14,000 rpm for three minutes. The supernatant was collected and analyzed spectrophotometrically at a wavelength corresponding to the maximum absorbance of the dye which is 530 nm. The uninoculated medium was used as control and the medium without dye was used as blank. The efficiency of the isolates to degrade/ decolorize Congo red was expressed as:

$$\text{\% Efficiency of degradation/ decolorization} = \frac{\text{Initial concentration of dye} - \text{residual conc. of dye}}{\text{Initial conc. of dye}} \times 100$$

Optimization of degradation of Congo red

The dye degradation was studied at various pH values (3, 5, 7, 9 and 11) and temperatures (4°C, 30°C, 37°C and 55°C) after 24 and 48 hours of incubation using a similar methodology, as described above.

Degradation of other dyes

The selected strain was grown in MSM(Minimal Salt Medium) media containing 100ppm of each of the dyes, Toluidine blue (Thiazine Dye), Methyl red(Azo Dye) and Acid orange 10(Azo Dye) for 24 and 48 hours at 37°C and pH7. The percent dye degradation was calculated after incubation.

Toxicity studies:

MTT Assay:

5000 MCF7 cells/well were seeded in a 96 well plate followed by overnight incubation in a CO_2 incubator maintained at 37°C. 100µl of different concentrations of Congo red dye or dye degraded metabolites (cell free supernatant) were added to each well (in triplets) in the presence of 100µl of complete medium (DMEM + 10% FBS) . After 48 hours of incubation, the supernatant was removed and 200 µl of freshly prepared MTT solution was added. The plate was incubated for 4 hours at 37°C. Then, the plate was

ISBN:978-93-84298-56-2

centrifuged at 2000 rpm for 5mins. MTT solution was discarded and 200 µl of freshly prepared 10% SDS solution was added to dissolve formazan crystals. The plate was incubated overnight. The absorbance was measured at 570 nm after incubation. Percent viability was calculated as described below:
% Viability = (Mean Absorbance of Sample x 100)/ Mean Absorbance of Control.

Phytotoxic Assay:
The mung (*Phaseolus mungo*) seeds were germinated in sterile 15 cm petri dishes, layered with sterile filter paper. Seeds were sterilized as described by Molla et al, 2001, before transferring to the surface of the filter paper in the petri dish. Approximately 20 seeds were placed on the filter paper which was wetted with 100ppm of Congo red dye, dye degraded product and distilled water (control) respectively. The plates with the mung seeds were incubated at room temperature and the germinated seeds were enumerated after seven days.

Strain Identification:
The morphological and biochemical characteristics of the dye degrading strain were studied. For genotypic characterization, the 24 hour old monoculture grown at 37°C on a nutrient agar slant was sent for 16S rRNA sequencing.

Statistical Analysis:
Data was analyzed by one-way ANOVA with a pairwise multiple comparison test. Readings were considered significant when P was <0.05 by using Sigma stat 3.5 and Microsoft Excel software.

RESULTS AND DISCUSSION

Isolation and identification of bacterial strains
Five bacterial strains from the effluent sample of Nandivli nullah showed decolorization of Congo red in 72 hours after initial enrichment and isolation, and were selected for further screening. The isolates were inoculated, using sterile toothpicks, into nutrient broth containing 100ppm of Congo red. One strain which showed maximum decolorization after 48 hours was selected for further study. The strain was identified as *Proteus mirabilis* on the basis of its 16S rDNA sequencing (Table 1).

Factors affecting degradation
The selected isolate was further investigated for the optimization of various environmental conditions for decolorizing the azo dye in liquid medium. The strain decolorized almost 100% of the azo dye in 48 hours of incubation at 37°C at a pH value of 7 (Figure 1).

Effect of pH
To study the effect of pH on dye degradation, different pH values ranging from 3 to 11 were used for incubation of the selected isolate (Figure 2). Initially with an increase in pH value from 3 to 5, decolorization increased. No significant difference in degradation was observed in the range of pH 5 to 9 after 48 hours of incubation. Further increase in pH showed a negative effect on the decolorization capacity of the isolate.

Effect of incubation temperature
Four different temperatures (4, 30, 37 and 55°C) were used for assessing optimal dye degradation by the selected bacterial isolate. The data obtained made it evident that the isolate could efficiently degrade the dye over a wide range of temperatures from 30 °C to 55°C. However, the isolate could not degrade the dye at the low temperature of 4°C (Figure 3).

Degradation of other dyes
The selected strain showed 100% degradation of the dye Methyl red after 48 hours of incubation. The strain degraded 25.51±2.5% and 12.7±0.98% of Toluidine blue and Acid orange 10 respectively (Figure 4).

Toxicity test with the dye degraded product
Congo red and the degraded products (after 24 and 48 hours) were checked for cytotoxicity by the MTT assay. The IC50 value of Congo red dye was determined to be 15.62µg/ml in MCF7 cells after 48 hours of incubation (data not shown). Results indicated that degraded metabolites are less toxic to MCF7 cell line compared to

ISBN:978-93-84298-56-2

untreated dye. The dye degraded metabolites showed significantly higher percentage of cell survival rate compared to untreated dye ($p<0.05$) (Figure 5).

Similarly, phytotoxicity study was carried out with dye and its degraded metabolites using the seed germination assay. In the presence of Congo red alone, the mung seeds showed 6.6% germination, while the control (distilled water) showed 100% germination (Plate 1). The dye degraded metabolite (48 hours) showed 80% of seed germination after 7 days.

Textile effluent treatment and decolorization is a tedious task. Wide ranges of pH, salt concentrations and chemical molecules further extend the task. Among the most economically viable choices available for effluent treatment/decolorization are biological systems. The ability of microorganisms to degrade azo dyes is well known. However, very few organisms can tolerate a wide range of pH and temperature which is necessary for dye degradation in the harsh environment of industrial effluents. In the present study, the isolate showed approximately 100% dye degradation within 48 hours of incubation at a range of pH (5 to 9) and temperature (30 °C to 55°C), which is appreciable.

Proteus spp has been shown to degrade a wide variety of azo dyes in earlier studies .The majority of the azo dye-decolourizing *Proteus* species reported, are able to degrade dyes at pH values near neutrality. But the selected strain can bring about dye degradation over a wide range of pH and temperature and is additionally capable of degrading other harmful dyes. Moreover, it degraded the toxic azo dyes to a non toxic form, which was confirmed by the MTT assay and seed germination assay.

CONCLUSION

The microorganism, isolated from waters contaminated with textile industry effluents, showed the potential of degrading Congo red dye at concentrations usually present in textile effluents (100ppm). The organism was capable of degrading Congo red over a broad range of temperatures and pH. The MTT assay and phytotoxicity assay revealed that this strain brought about the degradation of the Congo red dye to products that were far less toxic than the original.

The strain was identified as *Proteus mirabilis*. Further research on this strain could explore new tools and techniques to evolve viable and eco friendly microbial solutions for treatment of dye containing industrial effluent.

ISBN:978-93-84298-56-2

Table 1: BlastN report

Query		Subject					Score			Identities			
Start	End	Description	AC	Length	Start	End	Bit	Raw	EV	Match	Total	Pct.(%)	Strand
1	1476	Proteus mirabilis strain BAB-199 16S ribosomal RNA gene, partial sequence	KF535110.1	1503	16	1491	2726	1476	0.0	1476	1476	100	Plus/Plus

Figure 1: Percent dye degradation by the isolate after 24, 48 and 72 hours of incubation.

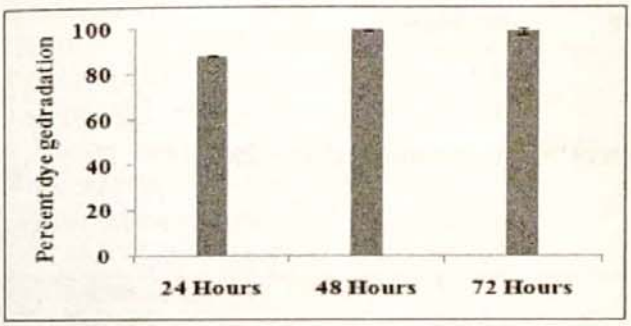

Figure 2: Dye degradation at various pH values

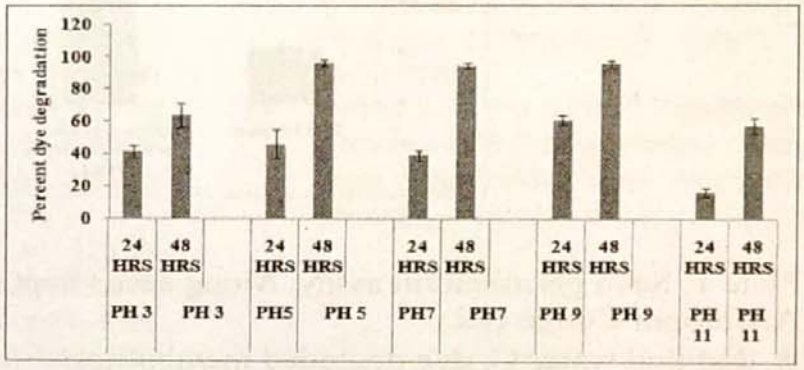

Figure 3: Dye degradation at various temperatures.

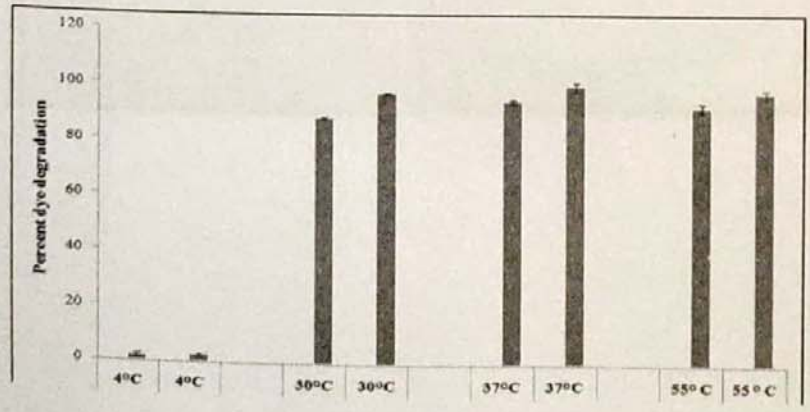

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Figure 4: Degradation of various dyes by isolate after 24 and 48 hours of incubation

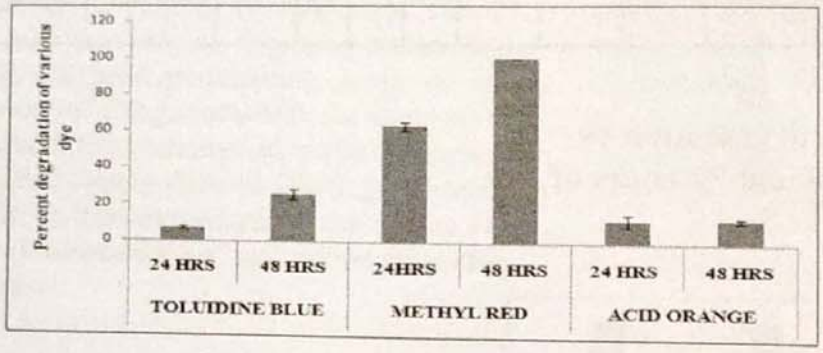


Figure 5: Cell viability measured by the MTT assay.

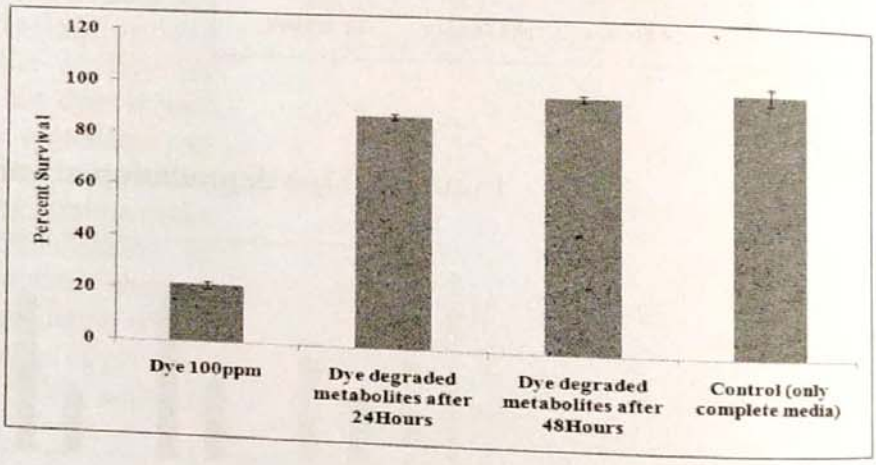
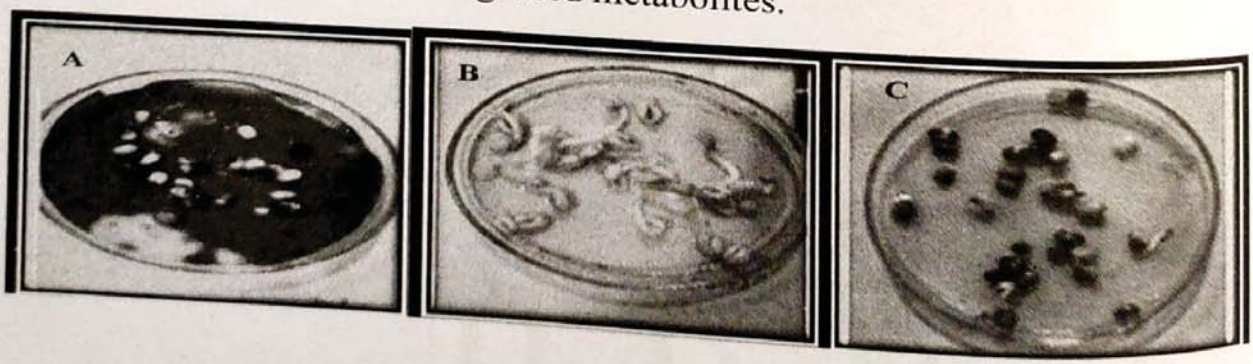


Plate 1: Seed germination assay: Mung seeds kept on Whatman paper with A.100ppm Congo red.
B. distilled water C. dye degraded metabolites.



ISBN:978-93-84298-56-2

Acknowledgement The authors thank all the staff members of the Department of Microbiology, St. Xavier's College, Mumbai, for their support.

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India's Foreign Policy

Nonalignment 2.0, Geopolitics and National Security

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the memory of
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a social worker, struggler, institution builder
and who was more than a father, a friend,
a companion...

7

Indo-Afghan Relations

Predicaments and Prospects

SHAZIA SHAIKH

It is a commonly established fact that Indo-Afghan ties have old roots dated back to the Mughal regime in India. Mughal emperors' descendants from Central Asia established their political control in India and enlarged it up to Afghanistan. British had strived hard to regain their control over Kabul and latter it had turned out to be a 'buffer state' between two great empires of the then British India in south and Soviet Union in north. Eventually, both Afghanistan and India under the British signed an agreement, popularly known as the Treaty of Rawalpindi, in 1919 recognizing sovereign status of Afghanistan.[1] Hence, Indo-Afghan ties, established in pre-independence period, entered into another era with the partition of India and formation of two nation-states. Though, with this, India lost its direct boundary with Afghanistan but this had not affected age-old ties between them. This can be substantiated from the statement given by the then Indian Prime Minister Jawaharlal Nehru on the occasion of the visit of Afghan Prime Minister Daud to India in 1959: "The partition of India separated direct boundaries and direct contacts between the two countries. But that made little difference to our age-old community of interests and our old friendship survived. And ever since then we have grown closer to each other for a variety of reasons, among them being mutual interest which is always a powerful reason."[2]

withdrawal of Soviet troops from Afghan land. As India was to restore its relations with Afghanistan, it had extended support to much fractured Najibullah regime. But it could not last long and soon the Rabbani government took over the rein of the country. India cemented its ties with new government and provided it humanitarian and financial assistance. But, as the civil war broke out in Afghanistan between warring factions, the regional stability perished.

However, the Soviet withdrawal from Afghanistan made major shifts in Indo-Afghan relations. Actually, prolonged Soviet presence in Afghanistan and the US interest in this affair had established Pakistan's legitimate role in Afghanistan. This new pattern had continued to be reflected in the successive formation of Afghan government. Pakistan openly defied its support to Rabbani government in connivance with his Prime Minister Gulbuldin Hikmetyar who had ISI connection.[7] Hence, Pakistan's overt domination in Afghanistan affairs provided major blow to India's interests and made profound repercussion on its bilateral ties.

Ultimately, Indo-Afghan relations enter into tragic phase with the dismissing of Rabbani regime and formation of Pakistan-backed Taliban rule in Afghanistan. Consequently, India had to closed its embassy in Kabul in September 1996. Right from the beginning, Taliban had maintained pro-Pakistan attitude and showed hostility towards India. In fact, major Talibani leaders had acquired training in Pakistani *madrasas* and also introduced radical Islamic *Sharia* rules in Afghanistan which was alien to Afghan Muslim majority country. During the Taliban phase, militants' escalation into Kashmir intensified much further. Taliban's overtly support to Pakistan's Kashmir cause endangered India's security concern.[8] It was during the Taliban rule when an Indian aircraft was hijacked in Kandhar and India had no option but to release Lashkar-e-Toiba chief, Azhar Masood.

Therefore, Taliban's incumbent regime in Afghanistan was a major challenge for India and in order to overthrow Taliban India had to join hands with Northern Alliance, a combination of non-Pushtoon groups, which had commanded northern areas of Afghanistan bordering the Central Asian states of Tajikistan

covering education, health care and educational research. The Indian government also adopted 100 Afghan villages for the purpose of rural development programme. One major Indian contribution was the construction of parliamentary complex at Kabul.[11]

India's role in the development of infrastructure in Afghanistan is crucial. It has supplied around 400 buses for public transport and handed over 300 military vehicles to Afghan National Army. In fact, India has helped to strengthen urban local administration of Afghanistan's major capital cities by supplying basic equipments to its municipalities. India has also generated electricity for local Afghan people by constructing Salma dam project in the Herat province. It has also enhanced Afghanistan's capacity in telecommunication and information and communication technology. India is actively involved in the capacity building of various Afghan officials. Every year large number of Afghan officials have been receiving training in India in various fields such as diplomats, police officers, judges, lawyers, airline officials, engineers, doctors, paramedics, school teachers, women entrepreneurs etc. In the area of institutional and human resource development, India has confirmed the annual award of 500 scholarships to facilitate and motivate Afghan students to study in the universities of India. India's aid also includes rejuvenating health sector in Afghanistan and for this purpose it had set up Indira Gandhi Institute for Child Health where Indian doctors have been giving treatment to more than 1,00,000 patients every year across Herat, Mazaar-i-Sharif, Jalalabad and Kandhar.[12]

Ever since the demise of Taliban, India had urged to increase its investment in Afghanistan and also bilateral trade. In 2003, during Karzai's visit to New Delhi, both India and Afghanistan for the first time had signed preferential trade agreement and also prepared list of commodities to be exported from one side to another side at concessional rates in the midst of greater difficulty of trade routes.[13] India's zeal to explore a new avenue is evident from the construction of strategic road across Zaranj-Delaram Highway. This road is significant in connecting India to Afghanistan via Chabahar port of Iran and is the shortest route for Indian goods to reach Afghanistan.

takes into account what they want.[16] Indian movies and songs have served crucial cultural links between India and Afghanistan. Large number of Indian movies and songs are exported from India due to its expanding demand in local Afghan market. "Indian Idol" is one of the famous TV programmes, which is seen there. Hence, it can be said that Indian cinema has become a powerful cultural tool in the hands of Indian diplomacy. India is basically capitalizing on this cultural link to develop its soft power to intensify people to people contacts and winning hearts of local Afghan people.[17]

In a nutshell, India's utilization of soft power in Afghanistan has deepened the goodwill and strengthened the mutual trust between two nations. India did not engage itself militarily in post-9/11 Afghanistan and thus easily avoided the risk of huge cost and instead diversified its major contribution for the redemption of war-affected region. India's soft power in Afghanistan has set the stage for ever expanding political and diplomatic rapprochement. This has also helped India to formed realignment with the major stakeholders in Afghanistan including Taliban. Though India had officially endorsed Northern Alliance against Taliban but given the USA's war withdrawal strategy, it can no longer remain indifferent to Taliban. In fact, not only Taliban has also positively acknowledged India's developmental role in Afghanistan but also appreciated it for neither reinforcing nor participating in America's war in Afghanistan. Hence, soft power has credibly helped India to win the confidence of major sections in Afghanistan and also mould the attitude and perception of Taliban towards India.[18]

However, India's developmental role has to face tough challenge in the midst of security threat due to prevailing standoff between NATO/ISAF and Taliban. Thousands of Indian workers and personnel deployed for the cause of reconstruction and rehabilitation have been going through the fear of insecurity. Though India has deployed paramilitary forces to safeguard Indian workers but there is an increasing threat to their security, particularly in the aftermath of withdrawal of foreign troops. In 2008, there was a major terrorist attack on Indian embassy in Kabul which killed more than 58 people and injured around 170 people.[19]

opportunities to India. India looks upon Afghanistan to fulfil its growing ambition to explore better prospects with these countries and hence enhance its influence in these regions.

In the geopolitics of Afghanistan, one of the vital Indian interests is to transcend to mineral-rich nations of Central Asia and Caspian region. Soon after the disintegration of USSR and formation of these independent nations, India has enduring ambition to establish its ties with them. As India lacks any physical access to this region, Afghanistan can potentially fulfil this vacuum and would serve this greater Indian interest. Silk Route is traditional phenomenon, which in the modern period surpasses Turkey, Egypt, Iraq, Syria, Iran, southern Russia, Afghanistan, Pakistan, India, China, Korea and Vietnam, and also eastern Mediterranean, the Arabian Peninsula and Central Asia.[21]

Ever since the end of Cold War, major powers like USA, Russia, China, India, Pakistan and Turkey have been seeking to explore natural reserves of Caspian region but this would not be possible without Afghan connection. In 2011, on the sidelines of UN General Assembly, all these major countries had endorsed New Silk Road project which would involved a multi-billion dollar network of roads, railways and gas pipelines linking the resource-rich Central Asia with the continent's fast-growing economies. Subsequently, immediately aftermath, another round of multilateral talk held in Istanbul and Bonn to assess potential hurdles involved in New Silk Road. India's Foreign Minister S.M. Krishna had hailed that this project would develop the "building blocks of our vision for Afghanistan as a hub linking Central and South Asia through pipelines, trade and transit routes for the common good of the people of our region and the world."[22]

In pursuing this vigorously, India has already ratified and is eager to operationalize Tajikistan, Afghanistan, Pakistan and India (TAPI) gas pipeline project to accomplish its vital energy requirements. Furthermore, India is mainly reinforcing its ambition by undertaking road and railway networks across Central Asian nations to enhance its trade, reduce tariffs and boost its potential economy. In the present era, Silk Route is strategically important for both global and regional powers and

॥ गौरिगौरवम् ॥

Festschrift in the Honour of

Dr. Gauri Mahulikar

Publisher : Mohiniraj Enterprises
2/35, Hanuman Ramanand Society,
Sant Janabai Road, Vile Parle (East).
Mumbai – 400 057.
Cell.: 9820106862

Printed At : Omshubham Enterprises
3, Dhanraj Industrial Estate,
Sitaram Jadhav Marg,
Lower Parel, Mumbai - 400013

ISBN : 978-81-931877-0-8

First Edition : 29, August 2015
Sanskṛt Din, Śrāvaṇa Pourṇimā

Donation Price : ₹ 500/-

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Gautama's *Dhamma*, in a holistic approach- An impact on the *Gahapatis* and *Gahapatins*.

Dr Radha Kumar

Dr Nalinaksha Dutt says "Buddha's teaching is regarded by some as more ethical than philosophical."John Locke says "Every man carries with him a touch stone to distinguish truth from appearances." Every individual is born with a purpose, and has the innate capacity to realize the ultimate truth and to comprehend his larger connected with the cosmos. Indian culture was the efflorescence of such a social organization and Gautama in many ways was the torch bearer of this ideology. His method of philosophical understanding was more of a psychological analysis where he attempted to annihilate all illegitimate speculation. Rhys Davids says "Buddhism varies through slight degrees as the centuries pass by in almost every book. But the system created by early Buddhism is one of the most original in its fundamental ideas capturing the essential spirituality."

The prime message of Buddha was to make the whole humanity happy. Buddha taught man, the gospel of self help in his efforts to lead a noble life. He made men to tap the internal energy within."Buddha's Dharma is also known as *Śāsana* or teaching, a ruling or a command. This is often called as *Sattā* or *Śāstā* i.e. Teacher or spiritual commander"[1] His view was that, the entire world was not segregated into the world outside and inside. The divisions or the dichotomy existed only when we subscribe to the external chaos, totally neglecting the inner quietude. Buddhism strives hence to raise the moral standards of the society and to teach people to live rationally. Dr. L.M Joshi says," We can say that the word dharma stands in Buddhist literature for both the End and the Means. "Buddha's teachings begin with the fact of his enlightenment, a spiritual experience which cannot be put into words. Whatever doctrine there is, it relates to this experience and the way to attain it."

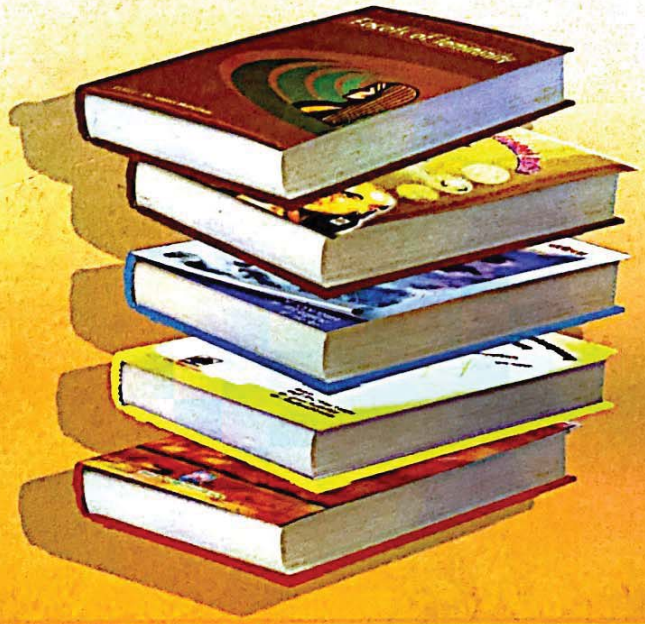
Gautama Buddha was great, not because he was a saint or a religious reformer but, because of his unflinching convictions. The Holistic teachings, of Gautama are further surmised by Aldous Huxley who says," Indian pacifism finds its complete expression in the teachings of Buddha,"

Another important aspect, seen in the society during the time of Buddha was the role and the importance played by the householders or *Gahapatis*. The uniqueness of the teachings of Buddha was that he integrated the householders in the course of his teachings. He made his thought process relevant to the conditions they lived in.

This book is the felicitation volume presented in the honour of Dr. Gauri Mahulikar. This volume is a compendium of research articles on variety of subjects ranging from Classical Sanskrit Literature, Modern Sanskrit Literature, Veda, Vedānta, Buddhist studies, Grammar, philosophy etc. This book also throws light on the contribution of Dr. Gauri Mahulikar to the field of Sanskrit in general and Department of Sanskrit in particular. Book unfolds the journey of Dr. Mahulikar as thorough researcher, an academician par excellence and able administrator. Not only students but also her family members, friends and associates have shared their impressions in this book in the form articles.

Apart from the biography, the volume includes *'Kathā Sanskritbhavanacī'* which is a special feature of this book.' This article highlights the efforts, dedication, love and labor of Dr. Mahulikar in making of 'Sanskrit Bhavan'.

This felicitation volume will be an intellectual treat for scholars, students and well-wishers. It will be a tribute in the form of ever fragrant bouquet to Dr. Gauri Mahulikar.



Slow Down, Banks and Role of Apex Banking Institutions in the Market Economy of India: The Way Forward

Editors
Satish Verma
Kulwant Singh

Chapter 20

Monetary Policy Framework And Challenges For Indian Economy

Aparna Kulkarni

Being an apex monetary institution, RBI is dwelling upon twin objectives to be served i.e., to contain inflation and sustain economic growth. Consequently for some of the last financial years, the growth performance of the economy is not encouraging. However, the inflation is considerably high, which ultimately affects the real growth rate of the economy. Obviously, the business world is not finding a way to get the pace for investment funds as the contractionary monetary policy framework is phenomenal. In the absence of transmission effect, there is no multiplier effect to help increase the growth rate.

On the real economy front, output and employment are also showing negative momentum as investment activities are at a slower pace, even though fiscal policy stance is expansionary with the aim to increase employment and output (e.g. MGNREGA). Clearly, the interplay between fiscal and monetary policy stance is not properly coordinated in order to face macroeconomic challenges of controlling inflation and sustaining growth. Also, at present, RBI is consistently trying to fight against the 'trilemma' of – "inflation – exchange rate management and economic growth". Recently, RBI has moved to the framework of rule based inflation targeting to fight against inflation; as a result, monetary tightening is continued.

At present, the development initiatives of RBI policy are revolving around some of the following factors:

- Strengthening the monetary policy framework.

branch expansion, [illegible] varieties of banks and entrants, moving foreign banks into better regulated organisational forms.

- Broadening and deepening financial markets and increasing their liquidity and resilience so that they can help allocate and absorb the risks entailed in financing India's growth.

- Expanding access to finance to small and medium enterprises, the unorganised sector, the poor and underserved areas of the country through technology, new business practices, and new organisational structures.

- Improving the system's ability to deal with corporate distress and financial institution distress by strengthening real and financial restructuring as well as debt recovery.

Along with the domestic initiatives, some of the international measures have also become a part of our monetary policy framework. Like, regulatory reforms agenda in the banking sector, also called the "Basel III" reforms are aimed at improving the banking sector's ability to absorb shocks arising from financial and economic stress; improving the risk management and governance framework and on strengthening the banks' transparency and disclosure standards. Minimum capital requirement, supervisory review and market discipline are the three strands of the third pillar approach of Basel II which RBI has started implementing in India in 2009. This shows that as a regulator and controller of market, RBI is a very ardent and investigative authority that everyone will accept.

There are two important dimensions to the conduct of monetary policy that need to be distinguished. The first is the adjustment of monetary policy instruments in reaction to changes in variables such as output and inflation.The second is the impact of the monetary authorities' actions on the real economy. Monetary policy transmission is the second dimension of the monetary policy decision-making process. It is the process through which monetary policy decisions are transmitted to changes in real gross domestic product (GDP) and inflation. The effect of monetary policy on real variables like, output and prices keeps on changing with time due to various kind[illegible] Therefore, for

a proper understanding of the transmission mechanism and to be able to understand the effects of monetary conditions on the real economy, feedback and interactions need to be carefully analysed. A successful monetary policy framework is the one which, on the one hand, takes care of the price stability by applying anti-inflationary policy and on the other hand, attempts to sustain the real growth by transmission effect by coordinating with fiscal policy. The present paper has attempted to study the policy pattern of RBI during the global crisis and how it has helped in protecting our economy from the slowdown. The policy response of RBI has played a crucial role during the crisis and hence, Indian economy could perform better than the crisis affected countries. The present paper is divided into three Sections. Section I deals with the severity of the effects of the crisis on global economy. Section II presents the analysis of RBI's policy to combat those effects and Section III describes the present policy perspective where, RBI is trying to maintain balance in price stabilization and economic growth.

Review of Literature

The policy response to the macro challenges, like, inflation and growth trade-off is one of the widely discussed topics amongst academia, industrial entities, researchers and policy makers as all of them find it relevant and apt. In the recent research, a paper by Nandini Sengupta (EPW, 2015), on the changes in transmission channel of monetary policy in India, shows that bank's lending channel is most effective channel for transmission so far and it is effectively used by RBI. In another article, Niruam Bajpai has shown the impact of global financial crisis on Indian economy and our policy response to it. In another working paper of IMF, Muneesh Kapur and Rakesh Mohan, 'India's macroeconomic performance: an assessment and the way forward', have also studied the present macroeconomic scenario in India and the policy response of RBI towards it. Some researchers have also argued that, as most of the economists are saying- there is no trade-off like situation in India. There is no clear sign of having inverse function of inflation and growth, so, RBI doesn't have to apply contractionary monetary policy in order to address the issue. Most of the researchers have accepted that our stringent monetary policy has protected us from

the global slowdown and it is still effective in combating the macro challenges of inflation and so on.

Global Economic Crisis and Indian Economy

The economic impact of global crisis on Indian economy can be seen in three different ways. First, the reduction in foreign equity flows – especially FII flows – impacted the capital and foreign exchange markets and the availability of funds from these markets to domestic businesses. Second, the shrinking of credit markets overseas had the impact of tightening access to overseas lines of credit including trade credit for banks and corporates. Both these factors led to pressure on credit and liquidity in the domestic markets with the knock on effects; and third, the fall in global trade and output had impact on consumption and investment demand. The cumulative impact of all this was a slowing down of output and employment. Despite the slowing down, India is still the second fastest growing economy in the world.

Also, the direct effect of the global financial crisis on the Indian banking and financial system was almost negligible, as the exposure to riskier assets and derivatives is limited. The relatively low presence of foreign banks also minimised the impact on the domestic economy.

Indian economy has also experienced moderation in growth. The growth rate of real GDP slowed down to 6.7 per cent (revised estimates) in 2008-09. Industrial production grew by 2.6 per cent as compared to 7.4 per cent in the previous year. In the half year ended March 2009, imports fell by 12.2 per cent and exports fell by 20.0 per cent. The trade deficit widened from $88.5 billion in 2007-08 to $119.1 billion in 2008-09. Current account deficit increased from $17.0 billion in 2007-08 to $29.8 billion in 2008-09. Net capital inflows at US$ 9.1 billion (0.8 per cent of GDP) were much lower in 2008-09 as compared with US$ 108.0 billion (9.2 per cent of GDP) during the previous year mainly due to net outflows under portfolio investment, banking capital and short-term trade credit.

The above mentioned facts show that the macroeconomic health of Indian economy was indicating that immediate policy response was the

need of the hour in order to fight against the situation. So, we come to the policy response of RBI as an apex monetary authority.

RBI's Monetary Policy Response and Global Crisis

Till August 2008, the RBI followed a tight monetary stance in view of the inflationary pressures arising from crude, commodity and food prices. In mid-September 2008, severe disruptions of international money markets, sharp declines in stock markets across the globe and extreme investor aversion brought pressures on the domestic money and foreign exchange markets. The RBI responded by selling dollars consistent with its policy objective of maintaining orderly conditions in the foreign exchange market. Simultaneously, it started addressing the liquidity pressures through a variety of measures. RBI then, adopted easy money policy by rate cuts and also auctioned repos, so as to maintain the liquidity flow in the market. The policy response of RBI during the crisis was manifold. As a monetary authority, a financial stabilizer, a debt manager, a foreign exchange manager and likewise, RBI had effectively tackled the issues.

The single most important concern that needed to be addressed in the global crisis was the liquidity issue. The RBI had in its arsenal a variety of instruments to manage liquidity, viz., CRR, SLR, LAF, Refinance, OMO and MSS. Through a judicious combination of all these instruments, the RBI was able to ensure more than adequate liquidity in the system. At the same time it was ensured that the growth in primary liquidity was not excessive.

The inherent synergies in its multiple roles enabled the RBI to ensure orderly functioning of money, foreign exchange and government securities markets while dealing with capital flows, managing additional government market borrowings and ensuring adequate credit to restore growth momentum. Both, macro prudential and micro prudential policies adopted by the RBI have ensured financial stability and resilience of the banking system. Also, the close coordination and interaction between the government and the RBI ensured that appropriate packages of measures were put in place promptly to deal with the crisis and restore the growth momentum.

The global crisis has taught us the lesson that for addressing such crisis like conditions, we need a policy coordination of both, monetary and fiscal policy. Otherwise, it becomes difficult to face the difficulties effectively. On this background, it is interesting to study the recent macroeconomic position of Indian economy in post crisis period and the policy response to it. Careful this analysis enables us to see whether those contemporary policy responses have long-term impact or we are skill surrounded by the same problems and the recovery is yet to be seen.

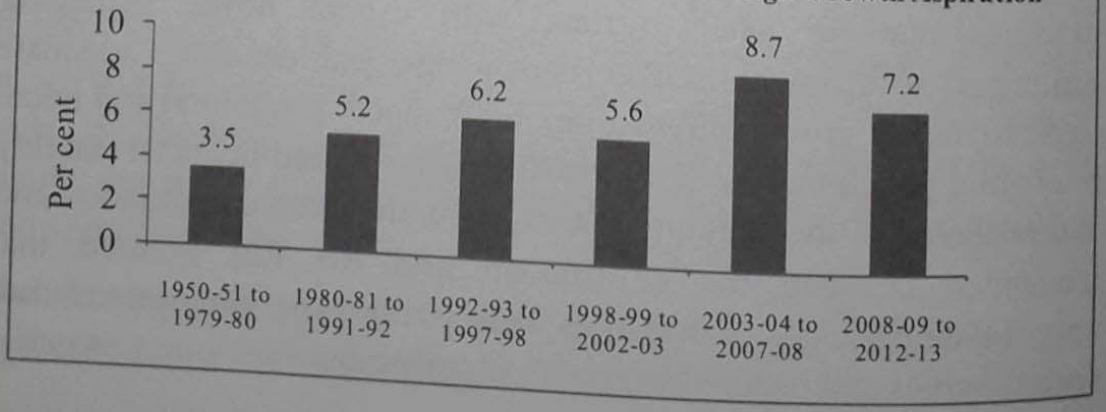
Indian Economy at Present and the Way Forward

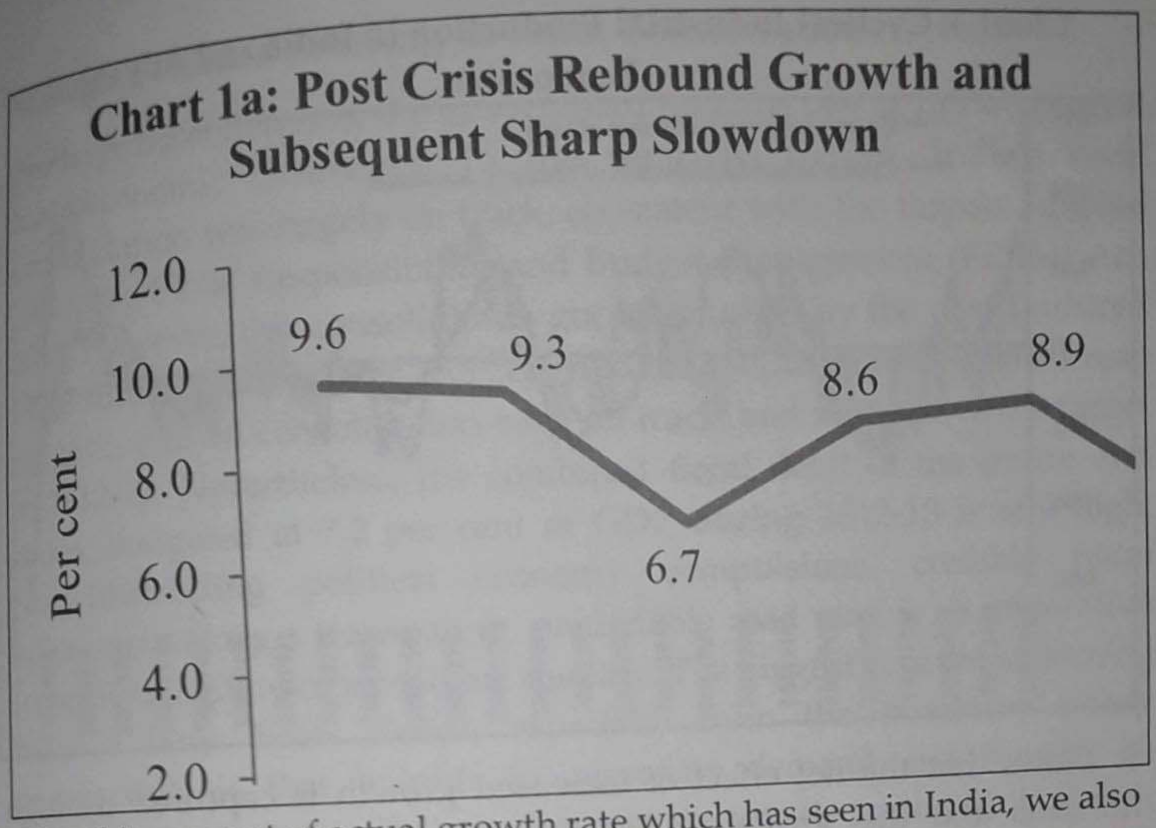
From the growth and stability points of view, Indian economy today is facing the following challenges.

Growth-inflation Dynamics

In the post crisis period, the GDP growth rate declined sharply, the probable reason for this could be a slowing of demand across the board. Private investment decelerated sharply, in part reflecting the global downturn, but largely owing to domestic factors. Business profitability was dented by tightening infrastructure constraints and increasing input prices stemming from high food and fuel inflation. Business confidence was hit by a rising fiscal deficit, vacillating commitment to reforms and governance concerns, all of which dampened investor perceptions on returns to investment. At the same time, inflation has worsened the situation. Demand and supply side factors have pushed prices upwards and this inflation growth dynamics has become critical. The following diagram further clarifies the argument.

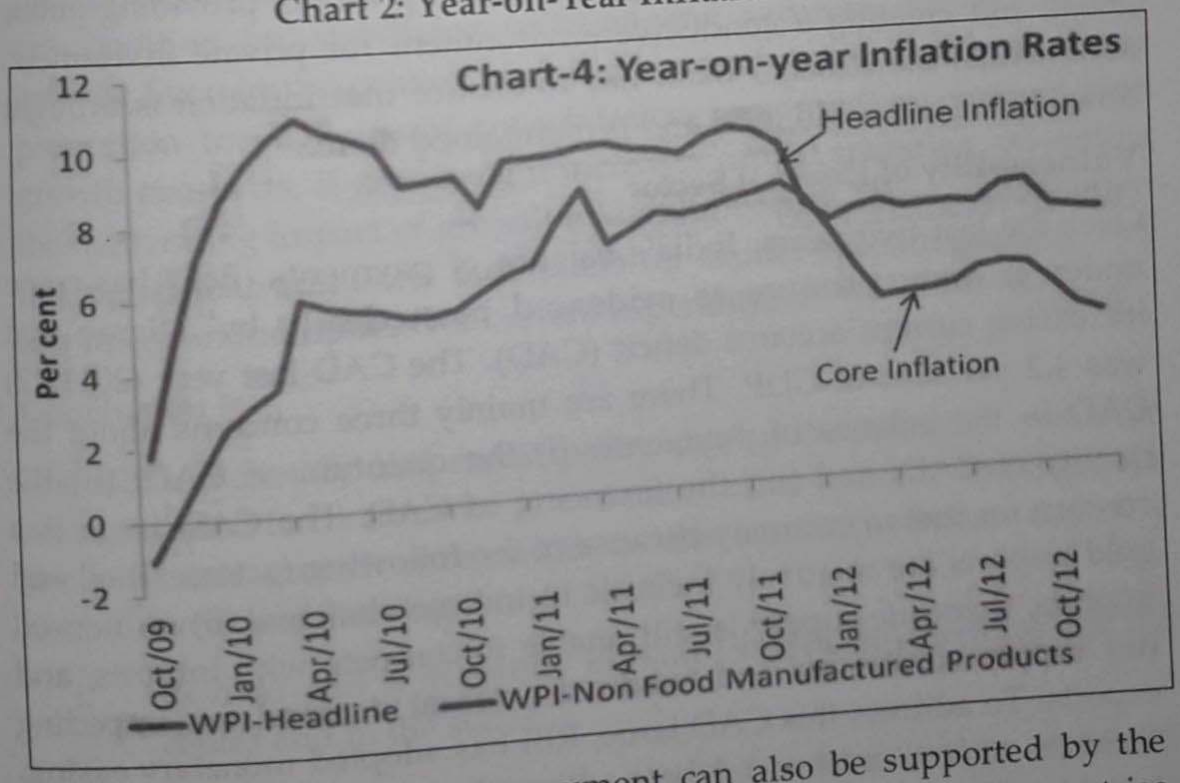
Chart 1: GDP Growth Hindu Rate to High Growth Aspiration





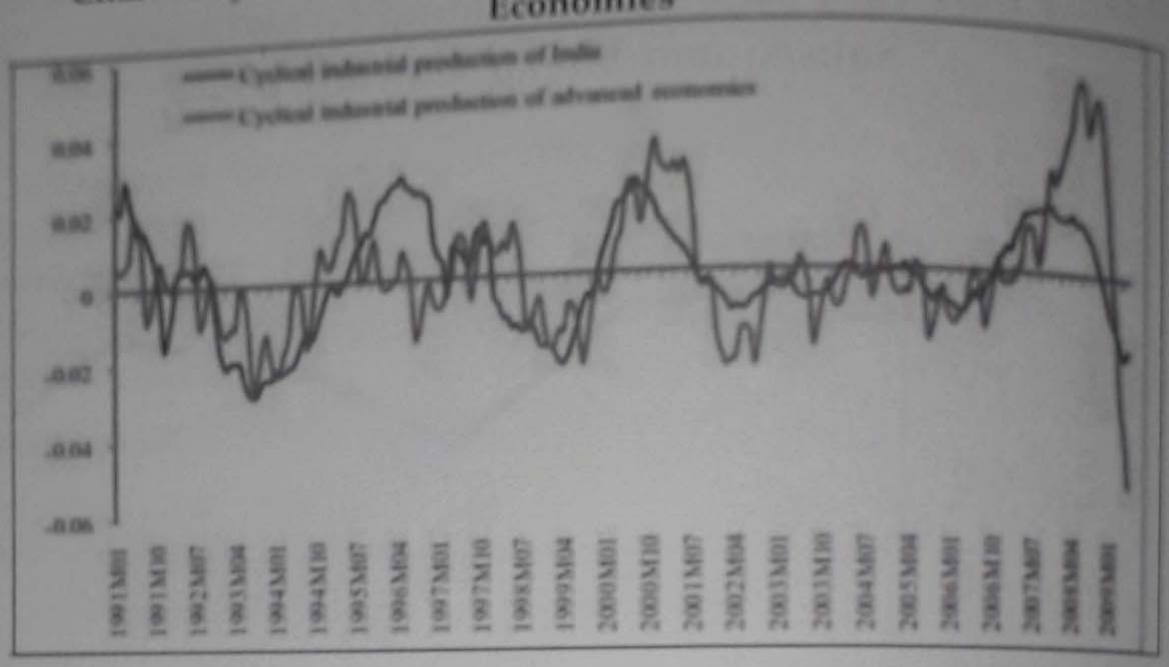
With this amount of actual growth rate which has seen in India, we also have to understand inflation pattern,

Chart 2: Year-on-Year Inflation Rates



Along with this, the above argument can also be supported by the nature of trade/business cycle in developing and developed countries as follows:

Chart 3: Cyclical Industrial Production in India and Advanced Economies



It shows that the net effect of increased growth is captured by high inflation and this growth inflation trade-off is the characteristic of Indian economy. To come over this particular challenge, it requires a supply side response from the government by way of providing public goods and creating a conducive environment for private investment. Meanwhile, the Reserve Bank has to ensure that inflation is brought down to the threshold level and is maintained there.

Vulnerability of External Sector

Over the last two years, India's balance of payments (BoP) has come under growing pressure as evidenced most clearly by a large and increasing current account deficit (CAD). The CAD last year (2011/12) was 4.2 per cent of GDP. There are mainly three concerns about the CAD in the balance of payments: (i) the quantum of CAD; (ii) the quality of CAD; and (iii) the financing of CAD. The CAD issue is a concern for Indian economy because of the following factors: (i) oil and gold imports are relatively inelastic to income changes; (ii) on non-oil imports, domestic supply is still unable to compete with imports, and (iii) supply constraints and subdued external demand are impeding exports. To address this CAD issue, RBI has adopted monetary easing, which is, in fact, causing a debate among the researchers. But, we have to understand that to improve our external sector performance, CAD has to be reduced.

Managing Political Economy of Fiscal Consolidation

The large fiscal deficit of the government remains one of India's biggest macroeconomic challenges. In the pre-crisis period, India's fiscal consolidation was largely on track, consistent with the targets adopted under the Fiscal Responsibility and Budget Management (FRBM) Act, 2003. However, this consolidation got interrupted by the crisis induced fiscal stimulus. Thereafter, the government adopted a revised road map for getting fiscal consolidation back on track, and adhered to the target in 2012-13. Nevertheless, the combined fiscal debit of the centre and states, budgeted at 7.2 per cent of GDP during 2012-13 is still high. Notwithstanding political economy compulsions, credible fiscal adjustment along a transparent, predictable road map is an imperative for growth and macroeconomic stability. The biggest concern stemming from a large fiscal deficit, especially from the monetary policy perspective, is that it adds to aggregate demand and thereby to inflationary pressures. By crowding out the private sector, fiscal deficit could also inhibit, if not impair, monetary policy transmission to the private sector. Credible fiscal consolidation is, therefore, a necessary pre-condition for stabilizing inflation and securing non-inflationary growth. Even in the context of decline in total public expenditure as a proportion to GDP, fiscal consolidation can improve medium-term growth prospects, if government increases capital spending, off-setting the moderating impact of growth in the short-term. These results reflect the higher long-run fiscal multipliers for capital expenditure and very low long-run multipliers for current expenditure.

Conclusion

The RBI's monetary and credit policy during the recession and even after, shielded India from the fate of many other nations. To bring back the pre-crisis growth momentum in the economy, Indian economy should have the following things:

i. Revival and a vigorous pursuit of economic reforms at the center and in the states;

ii. A major effort at raising the rate of domestic savings, especially by reducing government dissavings at the central and state levels through cuts in, and refocusing of, explicit and implicit

subsidies, stricter control over non-developmental expenditures, improvements in the tax ratio through stronger tax enforcement, and strengthening incentives for savings;

iii. Larger investments in, and better performance of, infrastructural services, both in the public and private sectors; and

iv. Greater attention to, and larger resources for agriculture, social sectors and rural development programs to increase employment, reduce poverty and for creating a mass base in support of economic reforms.

It is important to remember that the drivers of the India growth story – get up and go entrepreneurism, the demographic dividend, a large and growing middle class, the opportunity for productivity catch up, democracy and a decent legal system – are all intact. But the development won't take place inevitably. It will not materialise in the absence of vigorous and purposeful structural and governance reforms.

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CERTIFICATE

This is to certify that Ms. **Aparna Kulkarni** of **St. Xavier's College, Mumbai** participated in Two Days Regional Conference on **'Slow Down, Banks and Role of Apex Banking Institutions in the Market Economy of India: The Way Forward'** held at Centre for Research in Rural and Industrial Development (CRRID), Chandigarh on February 26-27, 2015. She presented a research paper entitled '**Monetary Policy Framework and Challenges for Indian Economy'** in the Conference.

It is further certified that Ms. Aparna Kulkarni also acted as a rapporteur for the Technical Session on **Banking for Development of MSMEs and Agriculture** in the Conference.

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INDIA-CHINA RELATIONS IN THE CONTEMPORARY ERA

(Opportunities, Obstacles and Outlooks)

Editors
Annpurna Nautiyal,
Chintamani Mahapatra

ISBN: 978-93-5128-059-0
Price : ₹ 1250

First Published, 2015

Published by

Kalpaz Publications
C-30, Satyawati Nagar
Delhi-110052
Ph. : 9212142040
E-mail: kalpaz@hotmail.com

Laser Typesetting: Quick Media, Delhi
Printed at: G. Print Process, Delhi

Cataloging in Publication Data--DK
Courtesy: D.K. Agencies (P) Ltd. <docinfo@dkagencies.com>

India-China relations in the contemporary era : opportunities, obstacles and outlooks / editors, Annpurna Nautiyal, Chintamani Mahapatra.
pages cm
Includes bibliographical references and index.
ISBN 9789351280590

1. India--Foreign relations--China--Congresses. 2. China--Foreign relations--India--Congresses. I. Nautiyal, Annpurna, editor. II. Mahapatra, Chintamani, editor.

DDC 327.54051 23

Contents

s long as China's military presence in Indian Ocean does not threaten India's national security, India will not take radical action against China.

Realists may think that the US is the biggest security threat for India in the Indian Ocean, because the US has the most powerful naval force in this region. India is not worried about the US threat because the two countries have built mutual trust through close naval cooperation. But despite this, it is still in India's interests to enhance naval cooperation with China in Indian Ocean. The Sino-Indian naval cooperation in the past was not very significant because China strategically did not give enough attention to India, and the military cooperation between the two countries was often influenced by their unpleasant political relations. However, the Sino-Indian naval cooperation presented optimistic trend, especially in 2012 for example, China, India and Japan agreed to synchronise patrols and allocate each country's escort resources in Gulf of Aden against piracy, and India and China also discussed the issue of resumption of their joint naval joint exercises. It is believed that the military mutual trust may naturally grow by continuous cooperation between these two because India-US military mutual trust have also taken 10 years of close cooperation to reach the present stage. Similarly Sino-Indian military mutual trust will also take at least 10-15 years of cooperation to make a significant difference. In this process, China's military presence in the Indian Ocean region will be enhanced gradually, which would help in forming a balanced power structure in this region. For achieving this goal the one thing which China needs to practice is that, it should keep her military capability and intentions as transparent as possible, and try to assure India that China's military presence in Indian Ocean will never be used to threatening India's national security.

22

Reviving Cross-border Trade between India and Tibet Autonomous Region through Tourism

Pratiba Naitthani

The bordering areas between Indian Himalayas and China's Tibet Autonomous Region are one of the most backward areas in terms on connectivity and economy. But these same areas used to be the hub of trans-border trade and also functioned as cultural interface before the Indo-China conflict of 1962. As tourism is emerging as the fastest growing industry, there is immense potential in promoting these traditional routes for cross border tourism. This is already happening along the traditional silk route between the Central Asian Countries and China. As India and China are gradually promoting cross border trade on the traditional routes, it is emphasised that the only viable product for trade along the traditional Himalayan routes is tourism.

Travel and Tourism are an important economic activity in most countries around the world. In 2012, the total contribution from Travel and Tourism to the world GDP grew by 3.0 per cent, which is faster than growth of the world economy as a whole (2.3 per cent), (World Travel and Tourism Council, 2013). Today, the business volume of tourism equals or even surpasses that of oil exports, food products or automobiles. In the current scenario, tourism has become one of the major commercial activities in international commerce, and has also become one of the main income sources for many developing countries. This growth goes hand in hand with increasing diversification and competition among destinations, (UNWTO, 2013).

In India, the total contribution of Travel and Tourism to GDP was INR 6,385.1 bn (6.6 per cent of GDP) in 2012. In terms of employment, Travel and Tourism industry supported 25,041,000 jobs (4.9 per cent of total employment) in 2012. In comparison the direct contribution of Travel and Tourism to Chinese GDP was CNY 1,361.9 bn (2.6 per cent of total GDP) with 22,756,500 jobs directly supported by the Travel and Tourism Industry. (1.00 CNY = 8.74 INR and US$.16). The border disputes between India and China are recent ones in comparison to historical trade and cultural relations since the 1st century. While the bilateral trade between the two countries shows a continuous upward trend, the defense budget of both the countries is still significantly higher (China US$106.4 billion, India Rs. 2,03,672.1 crore or US$ 37.4 billion), (World Travel and Tourism Council, 2013).

Ancient Trade Routes between India and Tibet Autonomous Region

India and China, two of the world's oldest civilisations and most populous nations, have coexisted in peace for millennia. In spite of their huge population they are the fastest growing economies. With the Himalayas, forming a formidable barrier between the two countries, they share a 4,500-kilometer-long (2,800-mile-long) border. Much of the cross border trade between India and China's TAR (Tibet Autonomous Region) was conducted through the high Himalayan passes. The same routes also facilitated in the cultural and religious exchange and pilgrimages, with pilgrims from India visiting Holy Kailash and Tibetan monks visiting Buddhist centres in the Gangetic planes. There were established trade norms and traditional institutional arrangements for the cross border management of trade. In fact, on the Indian side there exists a specific community, which had only one livelihood option that was trade with TAR. Known as 'Bhotiya', the settlement patterns of this community traditionally revolved around the trans-Himalayan trade routes to Tibet. Adapting a transhumant pastoralist life style, the Bhotiya community migrated to winter and summer settlements in the higher Himalayan region. The season between summers to autumn provided a limited window for cross border transactions. (Kainthola, 1994)

Using pack goats as a means of transportation, they ferried goods from the Indo-Gangetic plains to Tibet. In Uttarakhand,

Bhotiya community resides in the border districts of Ku and Garhwal, namely, Pithoragrah, Uttarkashi and Chamoli. Bhotiyas are further sub-divided into various ethnic grou hence the Bhotiya community of Uttarkashi is known as Jads, term derived from the river 'Jad Ganga' originating from their homeland. Jads are the followers of Buddhism. The Bhotiyas residing in the district of Pithoragarh have distinct identities as Byansi, Chaundensi, Darmi, Shouka and Rung Bhotiyas, while in Chamoli district, they have Tolcha and Marcha subgroups. In Uttarakhand's Uttarkashi district, the Jaadh Bhotiyas used the Nilang-Tsangchok La-Gartok route to access markets in Tibet. In Pithoragarh, trade was conducted through the Tawaghat-Garbyang-Lipu Leh Pass-Taklakot and Munsiari-Milam-Unta Dhura-Topidhunga- Gyanima routes. In Chamoli, the trade to Tibet was conducted from the Badrinath-Mana Pass-Totling-Gartok and Niti-Barahoti Dapa Gompa route. (Trail, 1992) Since the trade with Tibet was entirely in the hands of Bhotiyas (Walton, 1910), therefore, the British also being a trader community took keen interest in the Bhotiyas, but to suit their interest. As early as 1812 William Moorcraft visited Niti Vailey to investigate the sources of shawl wool for production in Scotland and Wales, (Brown, 1992). In fact, the British engagement with Nepal and consequent war was partly prompted by the desire to take control of the cross border trade routes between India and the TAR. According to Atkinson (1882), a conscious approach was followed during the boundary settlements with Nepal, to secure high Himalayan passes encompassing traditional trade routes with Tibet. It was the prospect of commercial intercourse with Tibet and not considerations of revenue from agriculture in the Himalayas that induced Lord Hastings to embark on the hill campaign. Its strategic location, from the view point of both defensive security and trade, played an important part in the evolution of British land policy in Kumaon, (Guha, 2008) 'The Trans Himalayan trade required an elaborate organisation and was based on fixed trading partner in Tibet known as '*Mitra*' or ceremonial friends. The partnership which ran through generations was legally binding through a contract called *'Gamgya'*. With the arrival of British the Bhotiya trade rose to new heights and the borax imported from Tibet was further re-exported to Europe, (Hoon, 1996). Bhotiyas used barter system, to export

od grains, *gur*, spices, rice, tobacco, cotton cloths, corals and eads and imported borax, salt, wool and gold dust in return. The salt brought by Bhotiyas from Tibet was high in demand. This continued for centuries till the closure of the borders between the two countries.

Tourism as a Product in Trans-Border Trade

As a step towards bilateral cooperation in trade, traditional trade routes were opened between the two countries. Opening of historical trade routes and symbolic revival of the traditional trade, pilgrimage to Mount Kailash and the trans-border Kailash Sacred Landscape Conservation Initiative between India, China and Nepal are definite signs of progress in mutual cooperation. However, relevance of traditional trade in terms of export and import of items needs a critical appraisal as the socio-economic conditions of the cross border communities has changed dramatically in between. Cross border tourism along the traditional trade routes is already on the active agenda of various Central Asian Governments. *For instance, efforts are already on to develop Silk Road Heritage Corridors' tourism strategy between Central Asia and China.* Recently with the support of ITB Berlin, the 3rd Silk Road Ministers' meeting brought together ministers and vice ministers of Tourism from over 20 Silk Road countries and international experts to discuss how to join forces to further raise the profile of Silk Road tourism, while safeguarding its exceptional heritage sites and intangible cultural heritage. Tajikistan has recently announced the opening of the Kulma pass on the border with China to international visitors, while Kazakhstan has stated its intention to pursue a visa-free Central Asia. (UNWTO, 2013)

Presently, cross-border trade between India and China's TAR takes place from the Nathu La and Lepu Lekh passes. The cross border Kailash pilgrimage is one of the most popular pilgrimage products in India which takes place from Kumaun in Uttarakhand. Cross border trade and tourism is one of the most prominent indicators of bilateral cooperation and trust between the neighbouring countries. In case of India, China and Nepal tourism is already expanding in the remote regions, for instance cross border tourism between India and Nepal and products like Motor Bike safaris between Nepal and the TAR. In view of the cost

effectiveness and relevance of export and import through high Himalayan traditional trade routes, tourism emerges as the most appropriate trade product for reviving the cross border trade between India and China's TAR. Major arguments in support of promoting cross border tourism through traditional trade routes are:

- The communities residing on both sides of the traditional trade routes do suffer from marginalisation due to remoteness, inhospitable terrain and lack of livelihood opportunities. Using tourism as a tool for poverty elevation through 'Community Owned Tourism' approach can help in addressing some of these issues.
- With the emerging majority of youth in the demographic profile, adventure sports are getting more and more prominence. Adventure tourism is witnessing the fastest growth in the overall tourism sector. The traditional trade routes reopened between India and TAR could be converted into top selling adventure tourism destinations in the world. These new products will directly benefit economies of both the countries apart from steering the overall dialogue towards peace and prosperity.
- While travelers from both sides are allowed to visit the border areas in both the countries, what remains to be covered are actually few kilometers or couple of days of high altitude trek between the two countries. A stage wise introduction of 'cross border' international tourism between the two countries and gradual up scaling appears to be the only way for harnessing the vast tourism potential of these regions.
- The folklore, travelogues and associated culture of the ancient Himalayan trade routes are part of the human legacy. While global adventure destinations compete with each other to attract visitors, appropriate packaging of adventure products along the ancient trade routes will elevate the status of these destinations above competition for decades.
- Further, the adventure tourism requires minimum infrastructure and capital investments as the essential

infrastructure is a present from the Mother Nature in the form of Himalayas.

Considered now as remote and on the periphery of civilisation, the villages and communities residing along these ancient trade routes in the past functioned as the centres of economic and cultural activities for centuries, these can again be made the main functionaries of this culture through reviving a vigorous trade and tourism in the present times also. The duration of closure of the trade and tourism is too short in comparison to the centuries of cross border relationships. Since tourism is the fastest growing industry in the world, it is high time for the Governments of India and the People's Republic of China to work out ways for converting these ancient trade routes into a hub of cross border adventure tourism. Provided economics is the priority, cross border adventure tourism along the traditional trade routes is the only option to ensure mutually shared portion of revenues from the emerging global tourism economy.

ACKNOWLEDGEMENT

Assistance of Dr. Sunil Kainthola, Director, Mountain Shepherds Initiative, in writing this paper is thankfully acknowledged.

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ELECTROCHEMICAL ENERGY STORAGE AND CONVERSION

SOLAR ENERGY CONVERSION AND STORAGE

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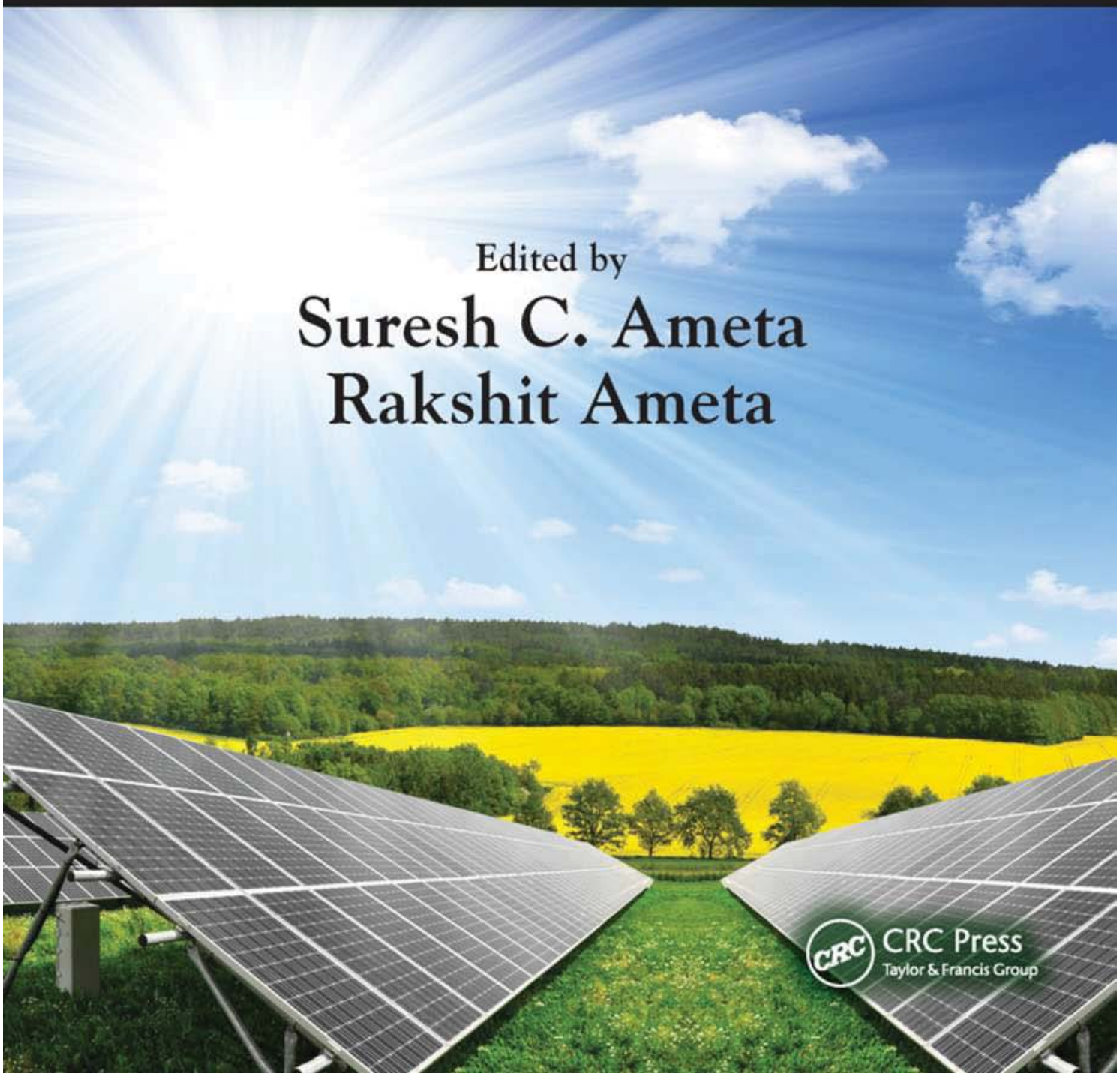

Edited by
Suresh C. Ameta
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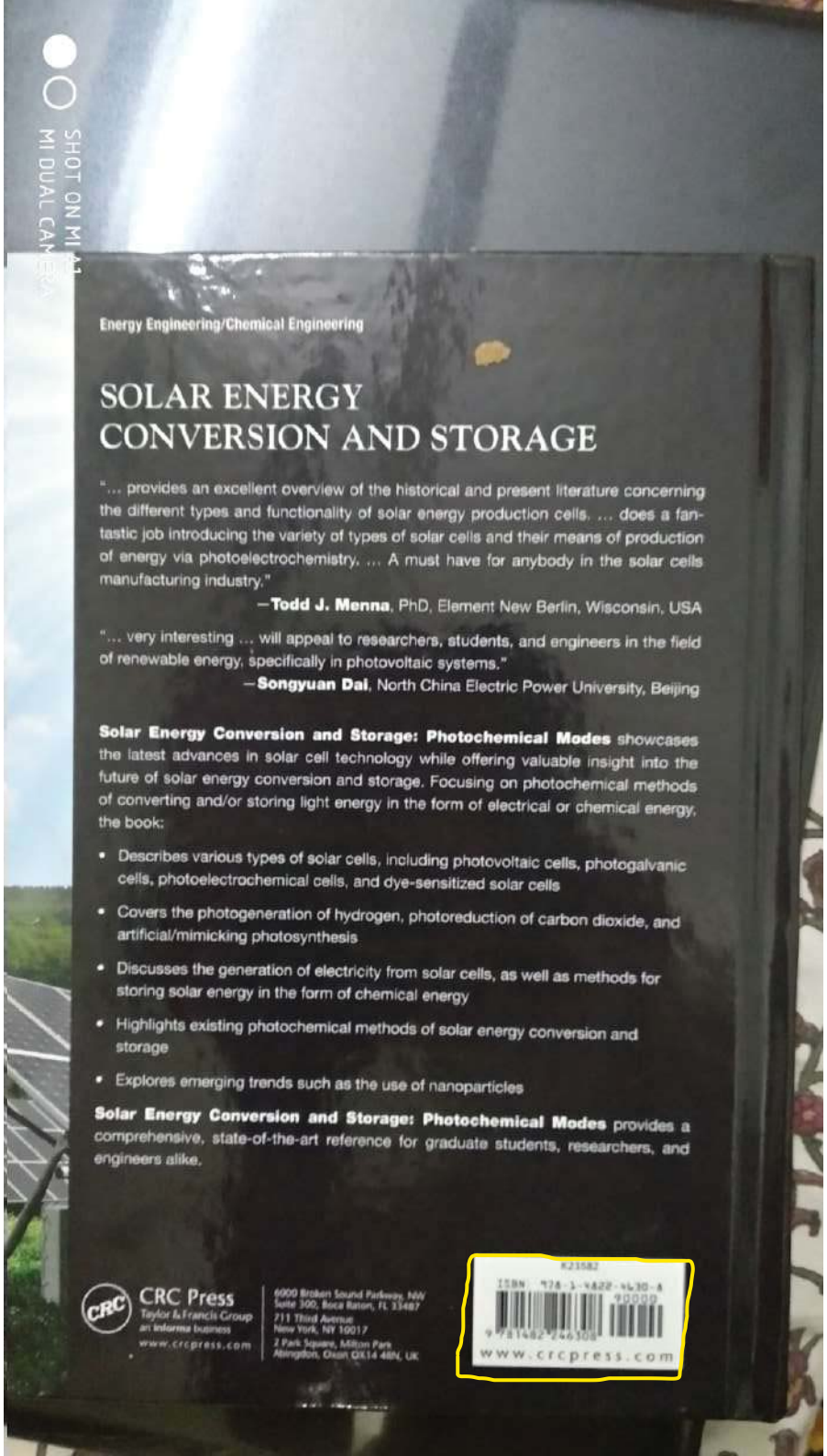

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K23582
ISBN: 978-1-4822-4630-8
90000
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Contents

7 Photogalvanic Cells

Yasmin, Abhilasha Jain, P. B. Punjabi, and Suresh C. Ameta

AU: Please provide full first name for the third author for consistency

CONTENTS

7.1 INTRODUCTION

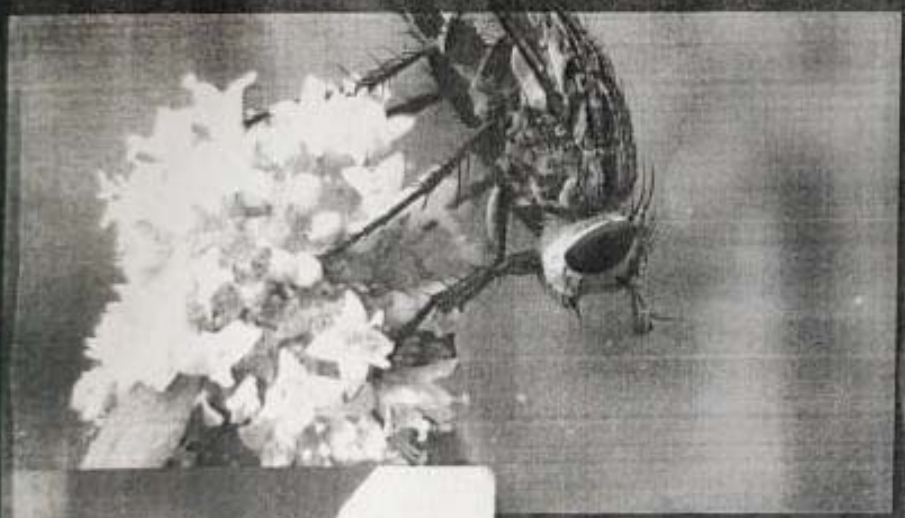
The world is experiencing adverse consequences from using current commercial energy resources that are based on fossil and nuclear fuels. Attention needs to focus on research to find clean and renewable energy sources. One suitable source of energy in this context is photogalvanic cells. They are also called liquid-junction solar cells. They can generate electrical energy from solar energy as well as electrochemical energy and provide the basis for a system with an energy-storage component.

Photogalvanic cells offer a promising area for exploration of the direct use of sunlight. Rideal and Williams (1925) first discovered the photogalvanic effect, but it was systematically investigated by Rabinowitch (1940a, 1940b) for an iron-thionine system. Weber and Matijević (1947) made an attempt to systematize the phenomena in terms of the *Becquerel effect*. Becquerel's photogalvanic effect has been thoroughly investigated on systems composed of different organic redox-dyes and organic acceptors, especially the speed of changes in potential and the influence of reducing and oxidizing agents.

Some photogalvanic cells using the iron-thionine system as the photosensitive fluid were built and tested to explore this suggestion. The observed maximum power conversion efficiency was 3×10^{-4}%, depending on light absorbed. The principal reason for this low efficiency may be polarization of the polished platinum electrodes. Coating these electrodes with platinum black reduced polarization sufficiently; as a result, it was possible to achieve an efficiency of 6×10^{-2}%, although this value was not actually observed. It may be possible to further increase efficiency by increasing electrode area and decreasing electrolyte resistance (Potter and Thaller 1959).

A photogalvanic device or cell is defined as a battery, where the cell solution absorbs light directly to generate photochemical species which, upon back-reaction through an external circuit in the presence of suitable electrodes, produce electrical power. It may store a significant amount of energy as chemical potential under open-circuit conditions and release it as electricity, when the external circuit is closed. This cell functions as a light recharged storage battery, if the chemical transformations occur in it without significant degradation over a number of cycles. Such photogalvanic cells based upon light-sensitive materials in solution are distinguished from photovoltaic cells, which are based on inorganic semiconductors (purely solid-state electronic devices). The photovoltaic devices depend on direct excitation of electrons and their separation from their geminate holes to produce electrical currents. They have a demerit that they lack inherent capacity for storage. All practical systems in use for direct conversion of sunlight into electricity utilize solid-state photovoltaic devices, particularly silicon p-n junctions.

Mutualistic Interactions between Flowering Plants and Animals



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KR Shivanna

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Published by Manipal University Press (MUP), Manipal INDIA
Admin Off: Manipal Centre for European Studies (MCES), Behind Post Office,
Manipal 576104 India

Title: Mutualistic Interactions between Flowering Plants and Animals
Editors: Palatty Allesh Sinu and KR Shivanna
Edition: March, 2016
Pages: 338
ISBN: 978-93-82460-26-8
Price: ₹ 950

Cover page design: Arvind N, Manipal University Press, Manipal

Cover page photograph credits: Palatty Allesh Sinu

Printed at Manipal Technologies Ltd, Manipal

Mutualistic Interactions between Flowering Plants and Animals

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Chapter 15

Plants Cry for Help upon Insect Attack and Parasitoids Come to their Rescue!!!

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Abstract

Plants are able to activate defence mechanisms against various forms of insect attacks. Insects produce various elicitors along with other components that induce defensive response in plants. The defence mechanisms could be direct in which the plants produce certain chemicals and/or structures to drive away or kill the insects attacking them. The defence could be indirect in which the plants call for help from other organisms by releasing some volatiles or other chemicals; the other organisms may be predators or parasitoids of the attacking insects. The following chapter elucidates tri-trophic interactions among plants; herbivores i.e., plant attacking insects and parasitoids of these herbivores. The emphasis is on indirect defence of plants in response to oviposition by herbivorous insects.

15.1 Introduction

Plants form the first trophic level in the food web. From microbes to man, many organisms feed on plants. Among these feeders insects are the most prominent ones. Approximately half a million species of insects are herbivorous (Dicke 2009). In tropical rain forests alone, insects devour 12 to 15 per cent of the total leaf area. All over the world, one sixth of the crops grown are eaten up by insects or fall prey to the diseases transmitted by them (Chapman et al. 2013). As a defence mechanism, the plants have evolved various means of perceiving and combating insect attacks on them. Once plants perceive insect attack they activate defence mechanisms which may be direct or indirect.

15.2 Forms of Insect Attack and Plant Responses

Plants not only sense the overt form of attack such as feeding damage by herbivore insects but also perceive subtle attack by herbivores even in the form of just touch and

egg deposition. Thus touching, egg laying and feeding could be considered as three forms of herbivorous insects' contact with plants. The following section briefly introduces these forms and plants' response to them. For more details refer to the review by Hilker and Meiners (2010).

15.2.1 Touch

Touch is the first contact of an herbivorous insect with its host plant. A plant may be touched by an adult insect to lay eggs and be fed on by the adult or its larval or nymphal stage. As the insects land and walk on the plants, they can be perceived by the plants as a result of increased pressure. Bristles present on insect tarsi may inflict scratches on the plants and such injuries are perceived by plants. Insects also leave behind their chemical footprints which can be sensed by the plants. The plants respond to these tactile sensations by rapidly changing cytosolic Ca^{++} signature (Haswell et al. 2008, Legué et al. 1997, Nakagawa et al. 2007) or by increasing the concentration of γ amino butyric acid (GABA) in the leaves (Bown et al. 2002; Hall et al. 2004). The leaves with high levels of GABA, when ingested by insects, are speculated to have detrimental effects on insect physiology by affecting their growth rate and survival. There is great scope to explore further the details of how plants perceive the touch by insects, and details of plants' responses and consequences of these responses on the ecology of plant and herbivore interactions.

15.2.2 Herbivore Oviposition

Egg deposition by herbivorous insects on plants is called oviposition. Herbivores usually glue their eggs to plant leaves with or without injury to the plant. Many studies have shown that oviposition-associated chemicals and/or injuries play a major role in plants' perception of egg deposition by herbivores. Once induced, the plants may defend themselves directly in the following ways. 1. Plants produce chemicals that repel the ovipositing insect females thus reducing chances of further egg deposition. The cabbage plant *Brassica oleracea* is known to produce oviposition deterrents in response to egg laying by the butterfly *Peiris brassicas* (Blaakmeer et al. 1994, Hilker et al. 2002b); 2. Plants produce ovicidal chemicals to kill herbivore eggs. Rice plants are known to produce chemical that kills eggs of plant-hoppers (Seino et al. 1996, Suzuki et al. 1996, Yamasaki et al. 2003); 3. Plants produce hypersensitive responses which cause eggs to detach from the leaves and fall off onto the ground. The larvae that hatch out from these fallen eggs rarely find their way back to the host plants and thus suffer an extremely high rate of mortality (Balbyshev and Lorenzen 1997, Hilker and Meiners 2006, Shapiro and DeVay 1987); 4. The plants produce neoplasms which raise the eggs from leaf surface and eventually detach them. Certain strains of the pea plant *Pisum sativum* are known to produce neoplasms in response to egg-laying by the pea weevil *Bruchus pisorum* and the cowpea weevil *Callosobruchus maculate*

Mastery Meets Mystery

Intersecting Science, Philosophy, Religion and Culture

Interdisciplinary Essays in Honour of
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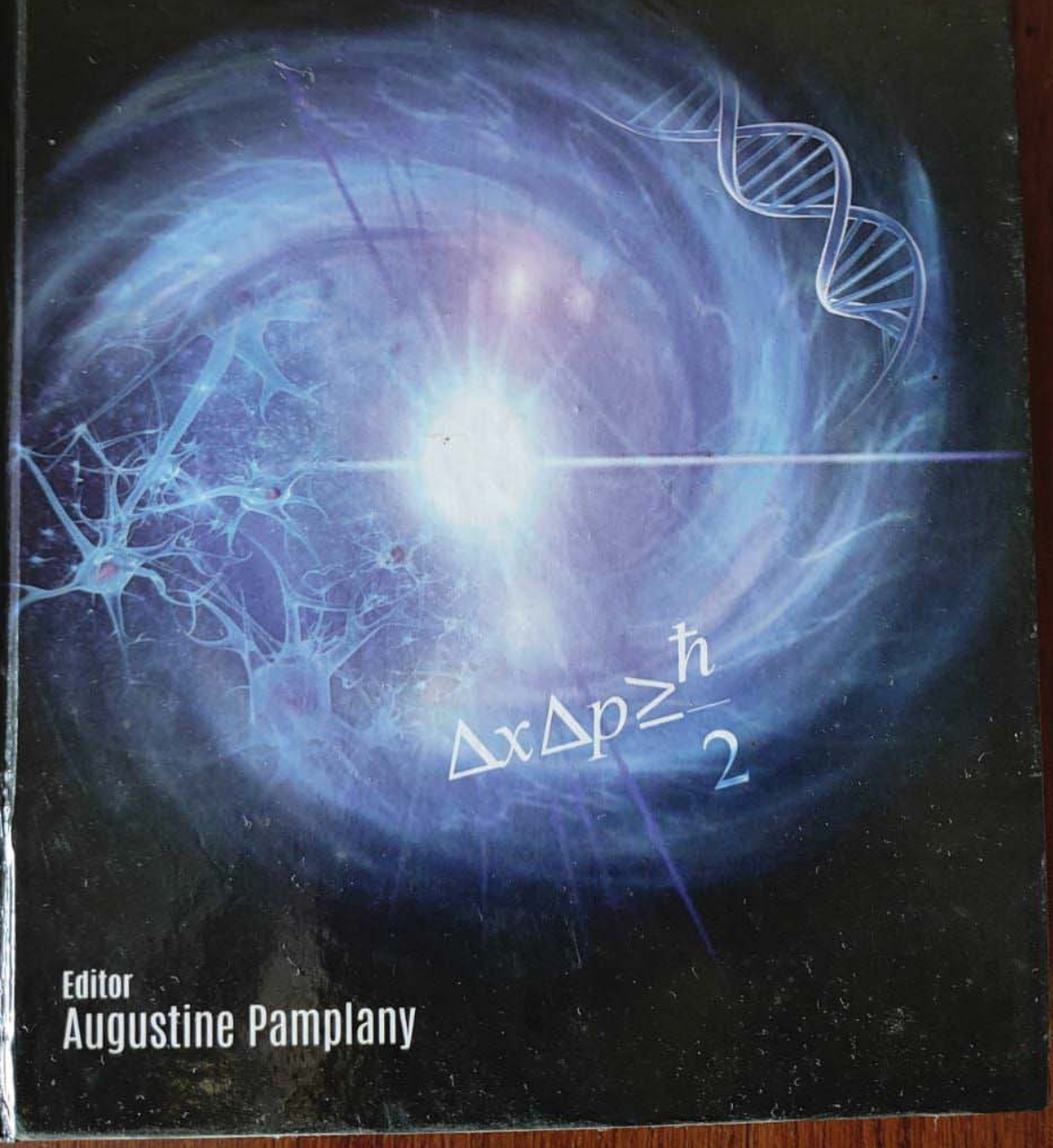

Editor
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SERIALS PUBLICATIONS PVT. LTD.

New Delhi (INDIA)

15

TECHNOLOGY AND BRAIN: WILL TECHNOLOGY EVOLVE A NEW WAY OF THINKING?

Roy J. J. Pereira,[1] Radiya Pacha Gupta

Introduction

This article though based in Neuroscience throws up many questions for philosophy and religion. Will the way we think change? If our brain is being restructured do we become different persons? If new synaptic links are constantly being formed, then what happens to memory? Will our memories be reworked? How then do we look at God? And how much of free will do we ultimately possess?

What is the Technological world? We are familiar with multichannel television, video games, movie players, internet, wireless, and the list goes on. Every single bit of information is now available to us, thanks to Google. Could the piano be called a technological invention? And, what about the drugs that we take? Being a professor of Chemistry and Neuroscience, the question does interest me. Can we also include drugs as

technology? We have drugs like *Paxil* as an antidote for shyness and *Ritalin* to improve concentration. An electronic chip allows a paralysed patient to move his limb while simply thinking about it. So, here when I am talking about technology, I am talking about both, the gadgets that we use and even some of the drugs that are used to "enhance" the life of human being. What then is the extent to which this gadget-filled, pharmaceutically enhanced 21st century affected our brains?

All of us are aware that technology is a mixed blessing. We could never imagine ourselves doing without it. There are a lot of positives and plenty of benefits that come along with it. Those students who are very much into technology become bright, nimble decision makers and at the same time intellectual light weights, easily distracted with a thirst for instant gratification. They find answers quickly having Information literally on their fingertips. On the other side, they lack deep thinking skills and do not allow time for reflection, analysis and critical thinking. Whilst visual skills have improved and they are able to process information better we have stagnation in literature as attention span shortens. Reading for pleasure enhances thinking, engages the imagination but video games and television don't have the same effect. So, what effect does it have on the brain?

Neuroplasticity

Till fairly recently it was believed that the brain was very much fixed for life after the first few years of growth. But more recently research has shown that even in adult life some neuronal connections are being made in certain parts of the brain. The term used for this is brain plasticity. Every neuron in the cerebral cortex has an estimate of two thousand five hundred synapses by the age of three and this grows exponentially to one thousand

Metaphysics? Categories of Second Generation Scientific Ontology (386 pp.), 2015 both from Peter Lang, Frankfurt; and about 20 philosophical articles in India. Research interests: cosmology, Western philosophies of physics, Being, God, knowing and logic, Vedântic and Mahâyâna metaphysics, and Christian and Indian mystic methods.

Roy J.J. Pereira teaches Chemistry and Neuroscience at St. Xavier's College, (Autonomous), Mumbai. He has been responsible for beginning the Neuroscience course at St. Xavier's College in 2012. He is also a visiting faculty member and a research guide at Jnana Deepa Vidyapeeth, Pune. His PhD involved the interdisciplinary areas of Chemistry and Neuroscience from Boston College, USA. He studied "Mind-Body Medicine" for one semester at Harvard University, Cambridge.

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Raphael Neelamkavil: After Ph. D. on causality in quantum physics, guided by Prof. Dr. Job Kozhamthadam at Jñâna-Dîpa Vidyâpîmh, Pune, he pursues Dr. phil. on causality at cosmic origins, at Universität-Duisburg-Essen, Germany. Publications: (1) *Causal Ubiquity in Quantum Physics: A Superluminal and Local-Causal Physical Ontology* (361 pp.), 2014, (2) *Physics without*

Prof. Job Kozhamthadam

Today, be it in physics, chemistry, life-sciences, nanotechnology, computer sciences, or information technology, an average inquisitive mindset with some philosophical taste can easily identify an irrefutable proximity between the technical and the conceptual, the physical and the metaphysical, the decoded and the yet to be decoded, and the natural and the supernatural. In tune with the interdisciplinary academic trend of our times, the essays of this volume attempt at exploring how the mastery of nature by science does spell out certain nuances of the mystery so vehemently wrestled with by philosophers and theologians. This volume identifies a few strands of such an unsolicited movement of the mastery of science to the mystery of religion in fields such as physical science, mathematical science, life science, neuroscience, etc. The domains of mystery in the Indian tradition and the present-day culture as the platform for this emerging fusion between mastery and mystery are also recognised herein.

Mastery Meets Mystery is fondly dedicated to Prof. Job Kozhamthadam, the pioneer of science-religion dialogue in India.

Mastery Meets Mystery

tersecting Science, Philosophy, Religion and Culture

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4830/24, Ansari Road, Darya Ganj
New Delhi-110 002 (India)
Ph.: 2324 5225, Fax: 2327 2135
www.serialspublication.com

Price: ₹ 1495/-
ISBN: 978-81-8387-762-6

Volume - 17
Number - 1, 2015

ISSN - 0972 1487

Journal of Microbial World

Published by :
Microbiologists Society

J. Microb. World, Vol. 17(No.1), PP: (119-126) 2015
Microbiologists Society
ISSN 0972 - 1487

MICROBIAL DEGRADATION OF AZO DYES BY ORGANISMS ISOLATED FROM A POLLUTED SOURCE

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ABSTRACT

Stability, color fastness and resistance to degradation, makes azo dyes, one of the most commonly and widely used dyes in the textile industry. But the recalcitrant properties of azo dyes, that make them suitable for the textile industry, make their removal from effluents highly difficult. The run-offs from these industries thus pose a threat to the environment due to the well documented toxic effects of these dyes. The degradation of azo dyes by microbial processes provides a favourable solution to reducing the levels of these dyes in industrial effluents. This study focused on isolating an azo dye degrader from a polluted soil source and studying the dye degradation by this organism. Organisms degrading a chosen azo dye were isolated and one isolate which showed the highest rate of degradation was selected for further study. Effects of various parameters such as pH, anaerobiosis, high salt concentrations and the presence of a heavy metal on dye degradation were analyzed. Thus the study succeeded in isolating an efficient azo dye degrader and optimized conditions for the dye degradation process during in situ effluent treatment.

Key words: Azo dye, Effluent treatment, Dye degradation

INTRODUCTION:

The many desirable properties of azo dyes such as bright color, water-fastness and simple application techniques, with less energy consumption have led to their widespread application in the textile industry (Rajeswari *et al,*. 2011). Of the total annual production of dyes, azo dyes account for 60-70% (Hao *et al.,* 2000). Of the many impurities present in wastewater, colour is one of the most disagreeable and is caused primarily by azo dyes. As some of the azo dyes or their metabolites like aromatic amines are extremely toxic and may have carcinogenic properties (Zhang *et al.,* 2010) reduction of azo dyes into amines in the gastrointestinal tract has also prompted concerns (Sirianuntapiboon *et al.,* 2007).

Many chemical and physical processes such as using activated carbon, flocculation with metal hydroxides, using ozone have been employed with very little success (Buthelezi *et al.,* 2012).

The harmfulness of azo dyes and metabolites has led to the possibility of using microorganisms for dye degradation. Biodegradation is now a widely accepted method and is a very useful way of

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