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〈Review〉

# Recent trend of chemical studies of fungicide in China

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**Abstract** : Recent progress of several kinds of compounds which have been synthesized or isolated from natural fungi for screening or conducting test as agricultural fungicides as well as some formulations for wood stain and decay control have been reviewed in this paper in China. Comments were pointed for Chinas further research and development of fungicides as well as pesticides.(Received February 12, 2002; accepted March 25, 2002)

Key words : China, Fungicide, Wood stain and decay.

## 1. Brief introduction to pesticide industry in China

0.42 million tons (100% active ingredient) of pesticide was produced in China in 1999 (Hu, 1999; Hu, 2000), the potential production in 1999 was 0.77 million tons, ranks the 2nd largest producing country in the world (Table 1).

Insecticide ranks the 1st production of pesticide in China(Table 2), organophosphorus, carbamate, pyrethroid are the main products of insecticide in China (Table 3). According to government policies, organophosphorus will not be developed any more in China for its high toxicity to human and environment.

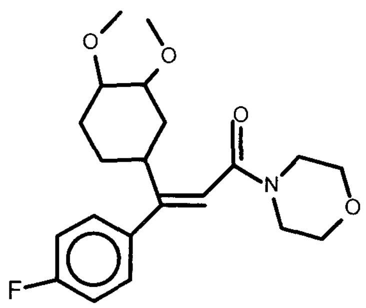
Copper sulfate was the only fungicide which could be produced in China in 1950. 50 Years later, China has a capability of producing varieties of agricultural fungicides such as amobam, benomyl, carbendazim (CBZ), chlorothalonil(CTL), EBP, isoprothiolane, maneb, mancozeb, metalaxyl, methylene bis-thiocyanate (MBT), thiobendazole (TBZ), thiophanate-methyl, thiram, tricylazole, triadimefon, and zineb, etc. The total production of fungicide is about 38,000 tons (100% a.i.) each year in China. Moreover some fungicides (biocides) such as validamycin A, blasticidin-S, kasugamycin, polyoxin, isolated from natural fungi rather than synthesized, are also commercially available in China.

## 2. Recent trend of development of new fungicides in China

### 2.1 Morpholine

**1** was developed by Shenyang Chemical Academy, and patented in China (CN 1043720), US and Europe.

**1** is much more effective to *Psudoperonospora cubensis* than other commercially fungicides. It is very effective to *Phytophthora infestans* and *Plasmopara viticola* conducted by Rohm&Haas company. **1** is a promising fungicide for its high activity, safety to crops, low dose and long effectiveness (The 9th symposium on Pesticide Science, 1998).




1 Z/E, SYP-L19

### 2.2 Organosulfur

**2** have good result for controlling stripe disease of rice and *Pyricularia orgzae,* etc (The 10th symposium on Pesticide Science, 2000).

The synthetic method and fungicidal activity of 2 and analogs have been patented in China (CN 1217331).

Study on the fungicidal activity indicated that the fungi of *Botrytis cinerea, Physalopora piricola, Cercospora beticola, Phoma asparagi,* and *Alternaia solani* can be totally controlled by 25 ppm of 3 (The 10th symposium on Pesticide Science, 2000).

4 (CAU-Wang) inhibited boll rot of cotton effectively at the concentration of 5 ppm (The 10th symposium on Pesticide Science, 2000).

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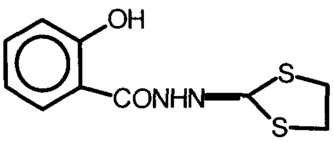

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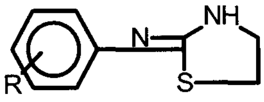

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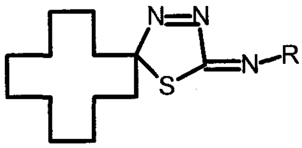

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**Table 1. Production of pesticide in China**

| Year/items | 1995 | 1996 | 1997 | 1998 | 1999 |
|---|---|---|---|---|---|
| Production Capacity (million tons) | 0.651 | 0.6933 | 0.7573 | 0.7616 | 0.77 |
| Actual production (million tons) | 0.349 | 0.3817 | 0.3945 | 0.4075 | 0.42 |
| Total Price (Billion US dollar) | | 2.07 | 2.38 | 2.68 | 2.76 |

**Table 2. Distribution rate of products of pesticide in China**

| Product distribution rate of pesticide (%) | Insecticide | Fungicide | Herbicide | Plant growth regulator |
|---|---|---|---|---|
| 1998 | 72.40 | 9.14 | 16.30 | 2.16 |

**Table 3. Distribution rate of products of insecticide in China**

| Product distribution rate of insecticide (%) | Organophosphorus | Carbamate | Pyrethroid | Other |
|---|---|---|---|---|
| 1998 | 64.65 | 4.50 | 3.64 | 19.45 |

**2.3 Triazole**

More than 2 dozen commercial triazole fungicides have been developed by more than 1 dozen companies in the world such as Philiph Dupher, Bayer AG, Simimoto, ICI, Ciba-Geigy, Rohm and Haas, Agrimont S.P.A., Rhone-Poulenc, E.I. du Pont de Nemours & Co. Inc etc. Among the commercial triazoles, Azaconacole (Jansen), Propiconazole (Ciba-Geigy), and Tebuconazole (Bayer AG) have been used for controlling wood mold and stain fungi. China Agricultural University and Nankai University have also conducted research of synthetic structure activity relation on triazole fungicides in recent years. For example, the fungicidal activity of **5** (Nankai-Li YC) against *Gibberella zear, Alternaria solan, Rhizoctonia sclani, Alternaria mali, Mycosphaerella arachid, Hypochuns sasakii, Botrytis cinerea, Sclerotima sclerotiorum* were determined, and some compounds of **5** have good fungicidal activity to the above fungi (Li *et al*, 1999). Some compounds of 6 (CAU-Chen) have good result for inhibiting wheat scab [*Gibberella zeae*] in the laboratory test, Compound 7 and 9 inhibit ring rot of apple and rhizoctonia rot of cotton effectively. 8 inhibits wheat rust effectively. But none of the above triazole compounds are potential fungicides which will be commercially developed in China (The 10th symposium on Pesticide Science, 2000).

**2.4 Organophosphorus**

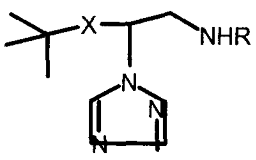
Some compounds of **10** inhibit *Pyricularia Orgzae* effectively at 50 ppm (CN 1217331; The 10th symposium on Pesticide Science, 2000). Some compounds of 11 inhibit *Pseudoperonospora cubensis* completely at 6.25 ppm in the laboratory test (The 10th symposium on Pesticide Science, 2000).

The fungicidal activity of 12 (Nankai-Tang) against *Gibberella zear, Alternaria solani, Alternaria mali, Botrytis cinerea,* and *Sclerotima sclerotiorum,* etc were excellent (Tang Chu-chi *et al*, 1996).

Some compounds of **13** are effective for controlling *Fusarium oxysporum* etc, they are also bactericides for controlling crown gall [*Agrobacterium tumefacciens*] in the soil (CN 1179427).

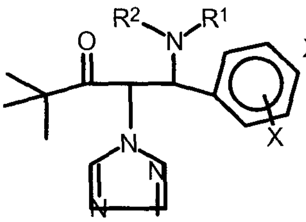
**2.5 Biocides from natural fungi**

**14** (9022A, B and C) were isolated from fungi *Stretomyces* sp. 9022. The structure was determined by Shanghai pesticide research institute and Institute of Physical and Chemical Research (RIKEN). **14**



R=substituted phenyl, alkyl,
5 or 6 ring hetercycliclyl
X=CO, CHOH

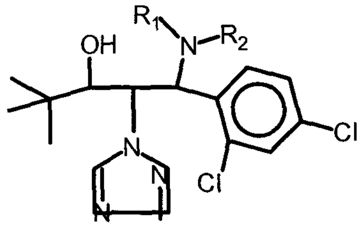
5



X=H,Cl,$OCH_3$

$R^1R^2N$=5,6 member cycloamine, $N(CH_3)_2$

6



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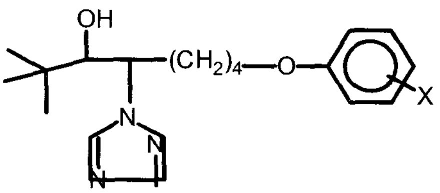

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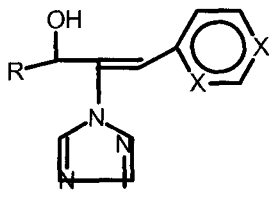

R=4-Ph$R^1$, $Me_3C$, $R^1$=F,Cl,Br,MeO,
X=C,N

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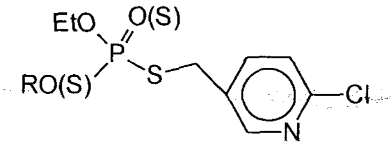

R=Et, Pr, CH2Ph,
substituted phenyl

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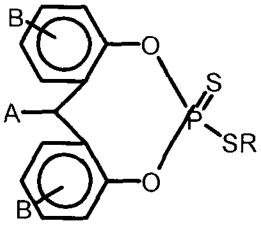
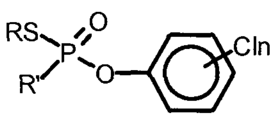


A=H, $CCl_3$;
B=$Cl_n$, n=2-3
R=alkyl, $CH_2COOR^1$, $R^1$=$C_1$-$C_4$ alkyl,
$CH_2CONR^2_2$, $R^2$=H, alkyl
$CH_2Ar$

11



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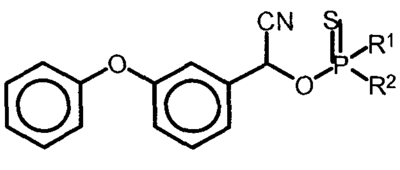
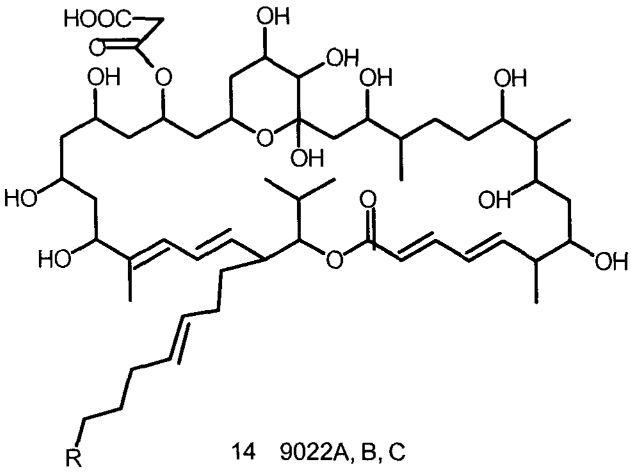


$R^1$=$C_1$-$C_4$ alkoxyyl
$R^2$=$C_1$-$C_4$ alkoxy,
$C_1$-$C_4$ amine, secondary amine

13

inhibits effectively some yeast and bacteria. For example, the MIC value of 9022A, 9022B and 9022C for *C. tropicalis KC-104, Cryp. neoformans KC-210, C. albicans KC-07, C. parapsilosis KC-110, C. glabrata KC-308,* and *S. aureus FDA 209P JC-1* are from 1.56 to 6.25 μg/ml, and MIC for *Asp. funigatus KA-01, Asp. flavus KA-06, T. rubrum KD-114, M. camis KD-305, M. gypseum KD-318, S. aurers Smith* are 12.5 to 25 ug/ml. 9022A and 9022B have excellent result for control gray mold, powdery mildew of cereals in the laboratory test (The 9th symposium on Pesticide Science, 1998).

Alternaric acid isolated from cultural solution incubated with *Alternaria solani* has high fungicidal activity against *Botrytis cinerea* and *Sclerotima sclerotiorum* (Li *et al*, 1997).



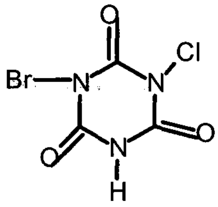

14 9022A, B, C

### 2.6 Flavanone

**15** are the mimic of **16**, a flavanone compound isolated from the rice tissue infected with *Pyricularia orgzae*. ED50 of compound **16** for *Pyricularia orgzae* is 15 ppm. The structure activity relation is under being conducted by Central China Normal University (The 10th symposium on Pesticide Science, 2000).

### 2.7 Amide

**17** is a patented compound developed by Nanjing Agricultural University and commercially available in China. It has good result for controlling bacteria, fungi and virus (The 10th symposium on Pesticide Science, 2000).

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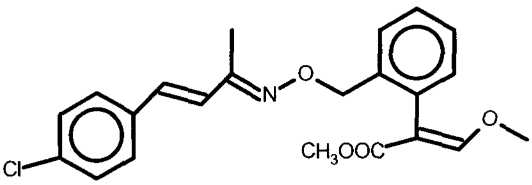
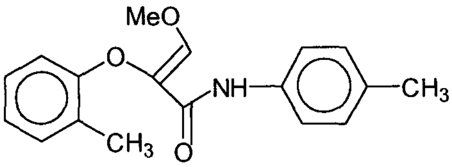
### 2.8 Strobilurin




18 SYP-Z071

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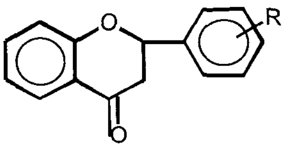
**18** is another fungicide developed by Shenyang Chemical Academy, patented in China (CN1062711C) and US. 18 is developed on the basis of lead compound strobilurin, which was isolated from natural fungi. Together with ICIA5504, ZA1963, BAS490F, SSF-126, 18 belongs to a same family of strobilurin (The 10th symposium on Pesticide Science, 2000).

19 is an analog of strobilurin which has fungicidal activity against *B. cinerae* at 50ppm in laboratory test conducted by Dr Wang Zhongwen of Nankai University (The 9th symposium on Pesticide Science, 1998).

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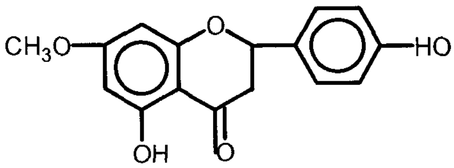


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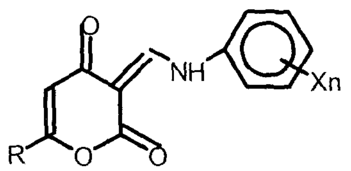
**Table 4 Inhibition ratio (%) of 20 towards fungi at 50 ppm**

| Cmpds | R | Xn | *P. Piricola* | *A. Solani* | *B. Cinerea* | *S. Sclerotiotum* | *H. Oryzae* |
|---|---|---|---|---|---|---|---|
| **20a** | Me | 2,6-Me2 | 9.0 | 86.3 | 0 | 28.6 | 42.9 |
| **20b** | Me | 2,6-Cl2 | 13.6 | 42.1 | 46.7 | 77.1 | 82.1 |
| **20c** | n-Pr | 2,6-Cl2 | 22 | 35 | 73 | 50 | 47 |
| **20j** | n-Pr | 2,6-Me2 | 40.9 | 57.8 | 20 | 54.3 | 46.2 |
| **20m** | Ph | 2,6-Cl2 | 31.8 | 42.1 | 46.7 | 80 | 60.7 |
| **20s** | Ph | 2,6-Me2 | 2.5 | 30.6 | 42.8 | 73.5 | 4.4 |

**2.9 Pyran-2, 4-diones**



20

Some compounds of **20** have fine fungicidal activity against some of the above fungi, for example, **20a** to *A. Solani*, **20b** to *H. Oryzae*, **20c** to *B. Cinerea*, **20b**, **20m** and **20s** to *S. Sclerotiotum*(Wang *et al*, 1999).

**2.10 2-substituted amino-4, 6-dichloropyrimidines**

The lead compound of **22** is **21** (iprodione), which was developed by Rhone-Poulenc in 1972 and commonly used for controlling gray mold and *S. Sclerotium*. Some compounds of **22** inhibit effectively gray mold *B. Cinerea* and *S. Sclerotium* at the concentration of 50 ppm, whereas some compounds of **23** have poor fungicidal activity against the above fungi (Yin *et al*, 1999).

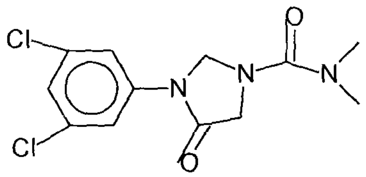
**2.11 Organotin**

**24** and **25** inhibit wheat scab and apple decay fungi effectively at the concentration of 50 ppm. The fungicidal activity of **24** containing pyridine is better than that of **25** containing indole (Li *et al*, 1996).

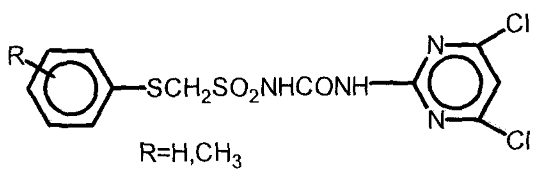
## 3. Development of fungicides for protecting wood in China

**3.1 Fungicides for controlling wood sap-stain and mold**

Sap-stain occurs commonly in wood, especially in sapwood at high moisture content. This stain degrades the commercial value of wood to its blue or brown color, rather than its natural white color even though it almost has no influence on wood strength. Many fungicides such as IPBC, CTL, MBT, CBZ, and copper oxine are used for mold and sap-stain control around the world. Commercially available agricultural fungicides rather than new synthetic compounds were



21 iprodione



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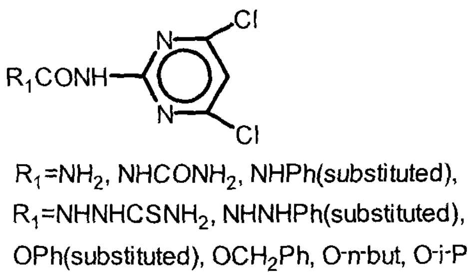

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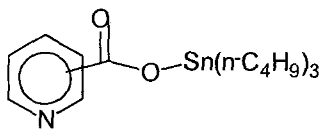

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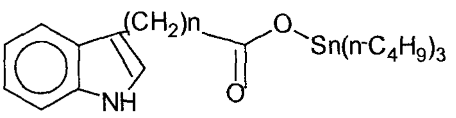


n=1,3

25

used for screening new formulations for stain control in China since this development is low cost and easy to reach the targets and achievements.

About 20 agricultural fungicides are commercially available in China. Some agricultural fungicides such as CTL, TBZ, MBT, and CBZ, etc, have been used as industrial fungicides in leather, paint, rubber, and textile industry. These fungicides have been widely used in many agricultural crops for preventing diseases. The most important advantage of these agricultural fungicides is: --Highly effective to most fungal species if they are properly mixed with; --Environmentally friendly.

Some commercial formulations containing CTL for controlling wood stain and mold fungi have been developed in recent years (Nicholas and Schultz; AWPA, 2000; Woods *et al*, 1994; Laks *et al*, 1992; Jiang, 1998; Jiang, 2001). CTL is a potential alternative preservative to sodium pentachlorophenate (NaPCP), which is strictly restricted or prohibited in some countries but currently is used widely in China, for controlling wood stain and mold. Research on CTL as wood preservative for sap-stain and decay control was conducted in China in recent years (Jiang, 1998; Jiang, 2001; Jiang, 2002; Lu *et al*, 2000). Laboratory evaluation indicated that the mixture of CTL and CBZ, 0.5% Tuffbrite C, 1.0% Tuffbrite 404, and 1.0% NeXgen inhibited the above mold and stain fungi species very effectively on rubberwood (Jiang, 1998). *Botryodiplodia theobromae*, a main blue stain fungi isolated from rubberwood, was inhibited effectively by 0.40% CBZ alone or the mixture of 0.5% CTL and 0.05-0.20% CBZ, but was not by 1.0% CTL, 0.20% CBZ and 1.0% NaPCP alone (Tables 5). Pilot test verified this result (Jiang, 2001).

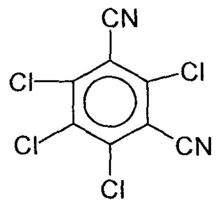
**Table 5. Comparison of the effectiveness of anti-sapstain treatments against *Botryodiplodia theobromae* on rubberwood**

| Anti-sapstain Treatment | Average |
|---|---|
| Untreated Control | 4.0±0.0 |
| 1%NaPCP | 3.0±0.0 |
| 1.0%CTL | 3.0±0.0 |
| 0.20%CBZ | 2.0±0.0 |
| 0.40%CBZ | 1.0±0.0 |
| 0.5%CTL+0.05%CBZ | 1.0±0.0 |
| 0.5%CTL+0.10%CBZ | 1.0±0.0 |
| 0.5%CTL+0.20%CBZ | 1.0±0.0 |

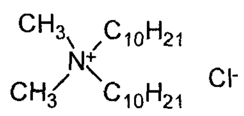
**3.2 Fungicides for controlling wood decay**

Formulation of CuO, $Cr_2O_3$, and $As_2O_5$ (CCA) is a main water-bore wood preservative used widely around the world. For example, about 16-18 million $m^3$ of timber is treated by CCA annually in US and the treated timber is mainly used for house construction. CCA faces environmental impact for chrome and arsenic in the formulation.

CTL, ammoniac copper quaternary ammonium (ACQ-B) and copper citrate (CC), which are included in American Wood Preservers Association (AWPA) Standard as wood preservatives in recent years (AWPA, 2000), are being conducted for protecting wood decay in China. They are the promising preservatives in China since they are non-chrome and non-arsenic and non-harmful to human and environment. The active ingredients of ACQ-B is: $Cu^{2+}$, dimethyldidecyl ammonium chloride (DDAC, 27), and ammonia; and CC: $Cu^{2+}$, citric acid, and ammonia.



26 chlorothalonil (CTL



27 DDAC

Laboratory evaluation indicated that formulations of CTL emulsion and CTL oil are effective to the above 2 fungi (table 6). Different retention of CC and ACQ-B are also effective to the fungi, even though

**Table 6. Weight losses of treated *Pinus massoniana* and *Populus tomentosa* inoculated with *Corious versicolor* (C. v) and *Poria placenta* (P. p)**

| Wood species / Treatment | Concentrations (%) | *Pinus massoniana* | | | *Populus tomentosa* | | |
|---|---|---|---|---|---|---|---|
| | | Retention ($kg/m^3$) | Weight losses (%) | | Retention ($kg/m^3$) | Weight losses(%) | |
| | | | C. v | P. p | | C. v | P. p |
| CTL emulsion | 1.20 | 9.2 | 0.2 | 0.5 | 7.0 | 5.9 | 1.7 |
| CTL oil | 1.08 | 4.3 | 9.6 | 7.6 | 4.5 | 8.4 | 9.2 |
| CCA | 1.50 | 10.4 | 0.3 | 0.2 | 8.8 | 0.7 | 1.2 |
| Untreated | 0 | 0 | 22.9 | 34.7 | 0 | 54.8 | 45.7 |

C.v.: a typical white rot fungus; P. p.: a typical wood brown rot fungus.

the weight losses of CC and ACQ treated wood were slight higher than that of CCA treated wood for the above fungi (Jiang, 2002).

The result of 3 year field trial at Guangzhou, South China indicated that the natural durability of CTL oil formulation is better than that of CTL emulsion since CTL emulsion is more movable from wood than that of oil formulation. ACQ and CC at the retention of 3.0-22 kg/m3 are effective preservatives for ground contact wood (Jiang, 2002).

Preservative fixation in wood is a main factor for effectiveness on controlling fungi, especially for the exterior wood such as in the circumstance of ground contact use. Primary result indicated that leaching rate of copper of CC treated wood is much higher than that of CCA and ACQ-B treated wood according to AWPA standard M11-87 (Jiang, 2002) and ACQ-B is promising preservative for ground contact use while CC could be used in less severe condition as ACQ-B and CCA-C. For example, the copper fixation rate in CC treated wood at retention range 1.9-17.8 $kg/m^3$ is from 70.20% to 84.65%. While the copper fixation rate in ACQ-B treated wood is at least 90.04%.

**3.3 Fungi resistant compounds from wood extracts**

Essential oil from buried wood of ancient Chinese fir is also decay-resistant. Laboratory test indicated that the resistance of buried wood against *Corious versicolor* and *Poria placenta* is better than that of Chinese fir from plantation. Probably because 42 compounds are isolated and identified from the essential oil of buried wood and only 29 compounds are found from that of planted Chinese fir by GS-MS (Lu, 2000).

## 4. Comments on the research and development of fungicides in China

China has conducted research on pesticide for 40 years. Several universities and research institutes such as Nankai University, China Agricultural University, Hunan Chemical Academy (Heli) and Shenyang Chemical Academy etc. have been involved into this research and development. The research and development of pesticide has been strengthened in recent 10 years in the following area: --Synthesis, structure-activity relationship; --Isolation from natural resource such as natural fungi and plant. Several new compounds as fungicide and insecticide as well as chemical hybridizing agent (CHA) have been developed in recent 10 years. Moreover pesticide formulation research has been also conducted. However, China legs behind the developed countries such as Europe and Japan and US in development of pesticides possibly due to the poor management by the government and insufficient financial resource since this development is much more commercial propose. In the future, enterprises and other private sectors in China should be encouraged to join this research and development, and share the investment, risk and profit.

## Acknowledgement

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## Literature cited

American Wood Preservers Association Standard, AWPA, 2000

Hu Xiaoxin (2000) Situation of Agrochemiclas in China, Pesticide Review.

Hu Zhisheng (1999) China Pesticide Handbook, Chemical Industry Press, Beijing.

Jiang M-L (2001) Pilot Study of Anti-sapstain and Anti-mold Formulations on Rubberwood Log and Timber, China Wood industry, 15(2):17～19

Jiang M-L, Highley T L, Ferge L, Woods T L. (1998) Laboratory Evaluation of Chrolothalonil Formulation for Stain and Mold Control on Rubberwood and Maple, International Research Group on Wood Preservation, IRG/WP 98-30175.

Jiang M-L, Wang P, Piao C-G, Li Z-B. (2002) International Research Group on Wood Preservation, IRG/WP 02-30279, Cardiff, UK

Laks P E *et al.* (1992) Efficacy of CTL against 15 Wood Decay Fungi. Forest Prod. J., 42(9):33～38

Li Bin, Lin Bingdong, Liu Changling, *et al.* (1996) Synthesis and fungicidal activity of 2-substituted amino-4,6-dichloropyrimidines, Hecheng Huaxue (Chinese Journal of Synthetic Chemistry), 4(2):176～179.

Li Shuzheng *et al.* (1997) the Anti-fungal Active Substance in Cultural Filtrate of *Alternaria solani*, Acta Phytopathologica Sinica, 27(2):161～165.

Li Yuchang *et al.* (1999) A Study of Biological Activity of the New Triazole Compounds, Acta Agriculturea Boreali-Sinica, 14(1):79～83.

Lu Xixian *et al.* (2000) Characteristics of buried wood of Chinese fir, Chemistry and Industry of Forest Products, 20(2):59～64.

Nicholas D D, Schultz T P. Biocides (1990) That Have Potential as Wood Preservation-an Overview. Wood Preservation Beyond '90

Tang Chu-chi *et al.* (1996) Studies on Synthesis of S-alkyl-O-polychlorophenyl thiophosphoric(-nic) Acid Derivatives and Their Fungicidal Activities, Chemical Journal of Chinese University, 17(3):414～418.

The 10th symposium on Pesticide Science (2000) Pesticide Science Society of China, March 27～30, Hangzhou, China.

The 9th symposium on Pesticide Science (1998) Pesticide Science Society of China, Shanghai China.

Wang Youming, Li Zhengming, Li Jiafeng *et al.* (1999) Synthesis and fungicidal activity of 3-anilinom ethylene-5,6-dihydro-6-alkyl(arkyl)-2H-pyran-2,4-diones. Chemical Journal of Chinese University, 20(10):1559～1563.

Woods T L, Laks P E, Fears R D. Wood (1994) Preservative Effectiveness of Combinations of CTL and Chlorpyrifos. Proc. Am. Wood Preservers' Assoc. 90:22～24.

Yin Handong, Zhang Rufen, Ma Chunlin (1999) Synthesis and application of tributyltin nitrogenous heteromatic carboxylate, fine chemicals, 16(4):6～9.