CHAPTER 5

DISCUSSION

5.1 Physico-chemical study of methamphetamine pills In Thailand, the methamphetamine pills (locally called "yaba") are very popular. It was found that all pills in the study were discoid in shape and convex at the surface, so center thicknesses are slightly greater than rim thicknesses. The pills are small enough to fit in the end of a drinking straw. In fact, illicit methamphetamine pills are often sold at retail packed in drinking straws. The methamphetamine samples obtained were mostly orange in colour. More finely, three particular orange shades predominated; all three shades were found in all studied provinces. It was observed that green pills would come with orange pills in a ratio 1: 100 to help with counting or marking. Regarding logos, many logos were found in the studied samples. The characteristics of methamphetamine pills from Southeast Asia, especially logos, are quite distinctive. These methamphetamine logos change from time to time. In 1996, the logo most observed was M/99 (34). This study found during the period October 2002- February 2003 that the most popular logo was WY (in four variants), followed by R, OK, 888 and w/99. The four variants of WY logo observed were wY, WY, wy, Wy. wY predominated followed by WY, wy and Wy. In the later period October 2003-May 2004, this study found that WY remained the most popular logo (again in four variants), but this time was followed by R, OK and 888. No samples with w/99 logo were included in the samples supplied by police for this phase of the study. wY still predominated, followed by wy, WY and Wy. In the two year periods of study, the three popular logos were wY, wy and WY.

The study of the physical characteristics of illicitly manufactured methamphetamine pills has the potential to yield key information about the manufacturing machines used to produce these illegal methamphetamines. The pills with WY, wy, wY and R logo showed greater variation in thickness and weight than did other pill logo groups. The weight of the pill is determined by the volume of the material which fills the die cavity and depends on the granule size and the void space. Therefore, the ability of the granulates or particles to flow freely into the die as

well as continuousness of movement of the granulates from the source of supply or feed hopper are important in insuring a uniform fill. The weight and thickness variations identified revealed possible problems in achieving uniformity of flow of granulates into the die. However the weight variation of the studied pills is not high. This fact suggests that all the pills included in this study might well have been manufactured by rotary tableting machines. Variation in pill thickness can indicate formulation or processing problems. At a constant compression load, variations in pill thickness are indicative of changes in die fill and consequently, pill weight, whereas with a constant die fill, thickness variation reflect changes in compressive force (35). Most samples studied showed high variation in hardness properties. The resistance of a tablet to chipping, abrasion, or breaking under conditions of storage, transportation and handling before usage depends on its hardness. Hardness depends on formulation, machine speed, particle size distribution of the granulation and the characteristics of punches and dies (33). Moisture can also affect tablet hardness. Since illicit methamphetamine pills are not stored in well-fitting containers, like pharmaceutical tablets. Conditions of storage of these pills can influence their hardness. The diameter and shape of the pills depend on the die and the punches selected for the compression of the pill. As there is a significant difference between diameters of methamphetamine pills bearing the wY logo compared to those with the wy logo, it is reasonable to infer that the size of punches and dies for the compression of the pills with wY logo and those for the wy logo pills are significantly different. This different would support a hypothesis that these two logos come from different manufacturers. Since wY logo and wy logo are the most commonly-found pills in this region, an inference can be drawn that there are two separate logo producing groups which are the methamphetamine manufacturers distributing methamphetamine pills in these areas.

Methamphetamine was the major ingredient found in the pills, with caffeine as an adulterant. Average contents of methamphetamine and caffeine were 21.76 – 22.79 % and 61.87 – 62.43 %, respectively. Amphetamine, ephedrine, theophylline and phenacetin were also found in some samples. Amphetamine and ephedrine might be left over from incomplete synthesis during manufacture. Impurities of the main

compound are commonly found in illicit amphetamine pills (11). Theophylline and phenacetin are sometimes present as adulterants in illicit amphetamine pills. In Poland it was found that phenacetin and caffeine were frequently used as adulterants in the street samples of amphetamine and their analogues (41). In the present study, within all WY logo samples, there were no differences between methamphetamine amounts amongst the variant WY logos. However, pills with 888 were observed to be higher in methamphetamine amount.

5.2 The study of disintegration and dissolution profiles As we know, illicit methamphetamine in Thailand is most commonly found in pill form. The pill is the most widely used dosage form because of its convenience and because of economic factors in the manufacturing process. For pharmaceutical-quality pills, it is imperative that the final product conform to tight specifications for qualities such as weight, dose uniformity, stability, strength, disintegration and dissolution rates, and it is known that all these are influenced by both the formulation components and methods of manufacture. The potential of numerous routine quality control procedures used in the pharmaceutical industry for application to the disintegration and dissolution profiling of methamphetamine pills is explored in this research, to see if these procedures could help develop a better picture of the methods and procedures used in clandestine methamphetamine laboratories in the region. Most methamphetamine pills collected into the study and included in the disintegration and dissolution study had smooth surfaces and a non-uniform colouring in the pill surface, referred to as 'mottling'. Only one sample had a shiny surface. Mottling arises through an unequal distribution of colourant on the surface of the pill. The illicit manufacturers, employing less sophisticated techniques, will often produced coloured pills with a mottled appearance and it may be indicative of the level of the expertise and the technique used by the manufacturer (13). The sample with a shiny surface might contain lubricant which can create a shiny appearance. Lubricant is used to reduce interparticulate friction, prevent adhesion of the powder to the surfaces of punches and dies, and facilitate pill ejection from the die. Many kinds of lubricant are used in pill manufacturing, examples being magnesium or calcium stearate and stearic acid. In 2000, 180kg of magnesium stearate, shipped from Bangkok, was

seized on suspicion the chemical was destined for illicit drug production in Burma (36). Magnesium stearate in the amount of 50 kilograms was seized with caffeine, acacia, ether, vanillin and food colouring agents at the border between Thailand and Myanmar, Mae Sod district, Tak Province in March 26, 2001 (37). It is probable that those seized substances were smuggled for use in methamphetamine production in clandestine laboratories. Based on these seizure cases, it appears that there has been an attempt to add lubricant which is magnesium stearate into the formula for illicit methamphetamine. However, most samples in the study did not show shiny surfaces, hence most manufacturers might still not use lubricants in their pill formulations.

It is accepted that in order for a drug to be available to the body, it must be in solution. Pills will be broken down into smaller particles or granules and become available to the systemic circulation. This process is known as disintegration. Many factors involving a pill's formulation and method of manufacture can affect disintegration. The disintegration times can be affected by the nature of the drug, the diluents used, the binders or amount of binder, as well as the manner in which these are incorporated into the pill. The disintegration time of a pill can be affected by the pore structure and bonding structure within the pill. A high porosity and the presence of large pores facilitate rapid water penetration into the pill with a subsequent rupture of bonds, followed by disintegration of the pill (38). All methamphetamine pills studied (across all logos), were observed to dissolve slowly, without breaking into fragments. It seems likely that the pills were manufactured without a disintegrant. Usually, as the applied pressure used to prepare a pill is increased, the disintegration time is longer (39). For pills compressed at low pressures, large voids can occur, so less time is required for the penetration of water into pill, which can lead to shorter disintegration times (17). In the present research, the pills with wY logo showed the fastest disintegration time followed by pills with wy and WY logos, respectively. It is possible that methamphetamine pills with wY, wy and WY logos were manufactured with differing formulations or methods of manufacture.

Disintegration time determination is a useful tool for production control, but disintegration of a pill does not imply that the drug has dissolved. A pill can have a rapid disintegration time yet be biologically unavailable. The dissolution rate of the

drug from the particles of the pill is the important factor in drug absorption and for many formulations is the rate-limiting step. Therefore, a dissolution time is more indicative of the availability of a drug from a pill that the disintegration test. In this dissolution study, methamphetamine content was determined at set time interval. From dissolution profile results, after 10 minutes methamphetamine from samples with the wY logo had been completely released whereas only after 30 and 45 mintues, was methamphetamine from the samples with wy logo and the samples with WY logo observed to be completely released. Generically identical pill products, manufactured by different pharmaceutical houses, were found to exhibit significant differences in the dissolution rates of their active ingredients (40). Factors that affect the dissolution rate of dosage forms include formulation factors and processing factors. Different types of excipient and compression force can cause differences in dissolution rate. From the study, the disintegration and dissolution profiles of methamphetamine pills with wY, wy and WY logo were different, which in fact is a possible indication that these pills came from different manufacturing laboratories.

5.3 Determination of dyes in methamphetamine pills Colourants are added to a wide variety of pills for aesthetic appeal and in order to distinguish one product from another. The illicit manufacturer is not bound by food or pharmaceutical safety laws, and may use anything from a food-colouring dye, readily obtainable at a supermarket, to a tin of fabric dye. Whichever type of dye is used, dye does provide another factor in the comparison of samples (42). It is indicated in this study that soluble food dyes are a very common form of colouring agent found in illicit pills, and the HPLC method has also been found to be of value in distinguishing the differences which occur in the number and nature of impurities present in these dyes from different manufacturers or in different batches (15). The HPLC system described can be used to separate the various components of colouring agents. The principle of this proposed method is that synthetic water-soluble colours can be adsorbed on polyamide in acid condition and can be eluted by mixture of a methanolic-ammonia solution. The eluted food colour fraction can be identified and quantitated by HPLC. Method validation results indicate that the proposed HPLC method is suitable for determination of food dyes in methamphetamine pills. In other countries, increasing

use has been made by clandestine manufactures of the insoluble "lake dyes" which are used in the pharmaceutical industry to prepare pills with an even colour distribution and a low tendency to mottle. Possibly fabric dyes could also be use as colouring agents for illicit manufacturing of methamphetamines because they are readily available in the market. However, in this study it was found that that only food dyes were used as colouring agents in methamphetamine pills seized in the areas involved in the study. Analysis of dyes can provide further evidence of linkage between samples. In further research, the impurities of food dyes in the pills could be studied in comparison with impurities in commercial food dye samples. The identification of dyes might also help to outline the supply chain for dyes used by illicit drug manufacturers.

5.4 Trafficking routes and distribution patterns of methamphetamine pills

Information from intelligence sources indicates that each manufacturer has a specific logo- -for instance, wY is produced by the United Wa State Army (UWSA). WY is connected with the Myanmar National Defense Alliance Army (Kokang Chinese). wy, Wy are the mark associated with the Shan United Army (SUA) or Former Khun Sa Army (43). The UWSA is the largest drug-producing and trafficking group in Southeast Asia, producing heroin as well as methamphetamine. UWSA produces methamphetamine pills embossed with the wY and 99 logos. When they first appeared, these logos were seen as being at the high end of quality for methamphetamine pills. However, over the past several years, other trafficking groups have been counterfeiting these logos as their own logos. Some sources assert that any one clandestine laboratory may produce methamphetamine pills with a variety of logos. In the present study, pills with the wY logo and with the wy logos were in the top two ranks followed by WY logos. In this present study, data showed that all three popular logos (wY, wy and WY) possess different disintegration and dissolution profiles, and notably, two popular logos (wY and wy) have a difference in diameter. It can be concluded with a high degree of certainly that methamphetamine pills with wY, wy and WY logos were manufactured with differing formulations or methods of manufacture. It could also be reasonably concluded that wY and wy logos were produced from different tableting machines. It is possible that these particular

logos might be manufactured from different clandestine laboratories or different producing groups. From this result, it could be concluded that each producing group has a specific detained logo. Each variant of WY logo could be linked to a distinct, separate manufacturer. As noted above, information from intelligence sources indicates that each manufacturer has a specific logo. It is likely from the data developed that the pills produced by UWSA are the most popular in this region, followed by pills produced by SUA and the Kokang Chinese's group, respectively.

The pictures of trafficking routes and distribution patterns of methamphetamine, which were drawn on the basis of identified physical and chemical properties of the samples, could show the connection of the samples. Among key findings are these: 29 samples having identical physical properties were seized in two different districts. In addition, 1 set of samples having identical physical and chemical properties was found in two different districts, Chiang Dao district in Chiang Mai province and Maesai district in Chiang Rai province. It could be probable that 29 samples which had identical physical properties might come from the same tableting machine. The 1 set of samples which had identical physical and chemical properties might come from the same batch in the manufacturing process.

Three border provinces—Chiang Mai, Chiang Rai and Tak—are regarded as the main smuggling routes for methamphetamine pills coming into Thailand. The relationship of physico-chemical properties of methamphetamine pills to trafficking routes from the main smuggling areas (Chiangmai, Chiangrai and Tak) was studied using predictive discriminant analysis. The predictive discriminant analysis is focused on classifying subjects into one of several groups. In this study, the discriminant analysis helps predict the smuggling sources where methamphetamine pills might come from. Distribution pictures of methamphetamine pills using GIS revealed the different patterns of methamphetamine pill distribution. The pills with wY logo seemed to be popular in the western areas in the North of Thailand whereas those with WY logo were spread throughout most of the areas studied. GIS can help develop more clearly defined pictures of distribution patterns of methamphetamine pills.

Identification of identical physical and chemical characteristics of samples can

help establish specific links between two or more methamphetamine samples and help draw pictures of trafficking routes and the distribution patterns of these pills. The predictive equations derived from discriminant analysis can help to identify the sources of unknown-source seized samples. Using drug characterisation and geographical information systems software to develop a picture of the distribution of seized methamphetamine pills in the northern region of Thailand has in fact resulted in a detailed and accurate drawing for the first time of the distribution profile of methamphetamines in this area. Drug trafficking routes are difficult to track. One tool is police intelligence. Drug profiling can be the other tool. These tools can complement each other, and strengthen each other. The sharing of information on the physical and chemical characteristics of seized methamphetamine samples could also become an important part of an international pro-active strategy for the control of the illicit drug trade. Drug profiling can be a useful tool to help law enforcement authorities to understand the patterns of drug distribution and to control drug trafficking networks.

Further avenues for research on narcotics in Thailand could take advantage of the techniques used in the study to help broaden the control efforts already in place. Continued development of this model methodology could lead to breakthroughs the control of other narcotic problems in Thailand. A database of drug samples should be develop to provide sample matching with reference samples to indicate of the drug source.