



... MICRO-GRAM ...

Volume I, No. 6

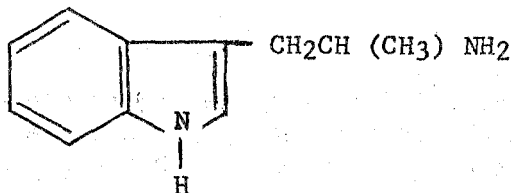
March, 1968

NEW HALLUCINOGEN

BDAC, New York reports possible use of "new" hallucinogen, "IT-290".

This apparently is alpha-methyl tryptamine, or 3-(2-aminopropyl) indole, also known as IT-403, U-14, 164E, and Indopan. The probable dose appears to be about 20 milligrams. Produces visions, flushing, crying aching and gastrointestinal activity. It reportedly produced increased serotonin in the brain. We have no analytical data on this material at this time.

It is listed in Aldrich Chemical Company's current catalogue at \$17 per gram.



CLANDESTINE LABORATORIES

We have been telling the agents and police officers in our schools about the potential hazards in raiding clandestine drug laboratories. We have advised them to secure the lab, and then ask for the services of a chemist to help identify and safely handle and store the chemicals and equipment.

Attached is a copy of our pamphlet "Notes on Clandestine Laboratories". This was developed by BDAC personnel in Los Angeles and Headquarters to assist agents and police officers. It may also be of value to you.

REFERENCES FOR SYNTHESIS OF SOME HALLUCINOGENIC AND STIMULANT DRUGS

Lysergic Acid Diethylamide (LSD)

Jacobs, Craig et al., J. Biol. Chem. 104, 547 (1934); W.L. Garbrecht, J. organic Chem. 24, 368 (1958); U.S. Patent Office: Patent #2,736,728 "Preparation of Lysergic Acid Amides", Richard P. Pioch, Indianapolis, Indiana, assignor to Eli Lilly and Co., 12-6-54.

CAUTION: Use of this publication should be restricted to forensic analysts or others having a legitimate need for this material.

Mescaline

Makepeace U. Tsao, J. Am. Chem. Soc., 73, 5495-5496 (1951)

Dimethyltryptamine (DMT)

Speater and Anthony, J. Am. Chem. Soc. 76, 6209 (1954)

Psilocybin

Hoffman, et. al., Helv. Chim. Acta, 42 1570 (1959)

Amphetamine Sulfate

Hartung, Munch, J. Am. Chem. Soc. 53 1875 (1931)

Hartung, J. Am. Chem. Soc. 50 3370 (1928)

Methamphetamine HCL

Ogata, J. Pharm. Soc. Japan, 451, 751 (1919)

DRUGS ON STREET

Recent purchases or seizures include STP in capsules, DMT powder, DMT impregnated on marihuana and tea, DET powder, and pink, truncated cone-shaped tablets containing 270 mcgs. LSD and 0.9 mg. STP.

SANSERT

Our Miami Resident Office has a report from the Fort Lauderdale, Florida Police Department that "SANSERT", Sandoz brand of methysergide maleate, is being tried as an hallucinogen by some persons. Each tablet reportedly contains 2 mg. of 1-methyl-lysergic acid butanolamide.

The product was approved as a new drug in 1966 intended for preventing or reducing the frequency of vascular headaches.

The Physician's Desk Reference lists contra-indications, warnings and side effects.

MORE ON PHENCYCLIDINE HCL ("PCP")

A special edition of Micro-Gram was issued on the "Peace Pill", January, 1968, giving the structure and characteristics of the compound.

Attached is a copy of additional identification data, sent to us by Mr. Paul M. Dougherty, Criminalist, San Mateo County Crime Laboratory, Redwood City, California. Mr. Cecil L. Hider and Mr. Steve P. McJunkins, Criminalists in Mr. Dougherty's Laboratory, developed the data and may have been the first persons to identify "PCP" in illicit use in the United States.

Mr. Dougherty sent us photographs of crystals, but we are unable to properly reproduce them in Micro-Gram. The men in the crime laboratory in San Mateo County deserve a "well done" for the excellent job they have done on the "Peace Pill".

We have reports that marihuana impregnated with "PCP" is being used.

METHYLPHENIDATE HYDROCHLORIDE, RITALIN (CIBA)

Over the past two years, we have received increasing numbers of reports of abuse of methylphenidate. (Chemical name: Methyl-alpha-phenyl-2-piperidineacetate hydrochloride).

Methylphenidate is a central nervous system stimulant used medically as a mood brightener, in chronic fatigue and in various psychoneuroses. It is also used in overdoses of barbiturates and other depressants.

It is reportedly being abused particularly among hard narcotics users. Drugstore burglaries frequently result in stocks of methylphenidate being taken. Narcotics users agree that methylphenidate has three properties:

1. It reduces the amount of heroin that has to be taken to produce the desired effect.
2. It extends the duration of action of heroin.
3. It minimizes the agonies of withdrawal when heroin is not obtainable.

The tablets are crushed, dissolved and then injected either in conjunction with heroin or alone. The drug when injected by itself produced a "flash", and results in a degree of euphoria similar to that produced by amphetamines.

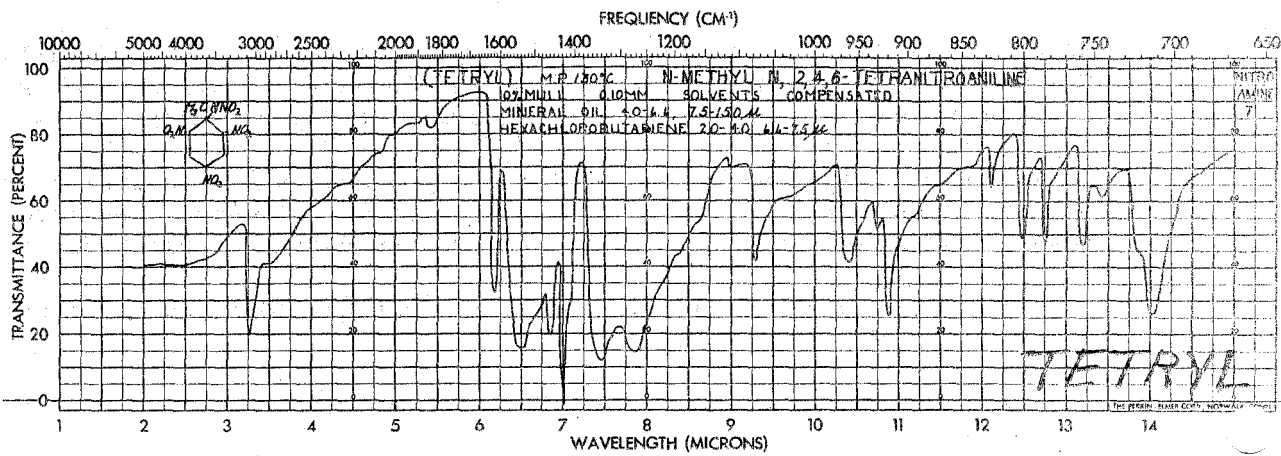
Although the major source of methylphenidate appears to be drugstore burglaries, a large amount appears to be smuggled into the United States from Japan and other parts of the Orient, where it is reported to be readily available on a non-prescription basis. It is believed to be brought into the United States by servicemen.

We would appreciate receiving any information you may have on the abuse or misuse of methylphenidate. Send it to Dr. George Spratto, Division of Drug Studies and Statistics, Bureau of Drug Abuse Control, 2221 Jefferson Davis Highway, Arlington, Virginia 22202.

TETRYL

We warned you about the explosive, Tetryl, in our last issue of Micro-Gram (No. 5)

The I.R. Spectra for Tetryl below, was furnished by Chemical Propulsion Information Agency, Applied Physics Laboratory, Johns-Hopkins University.



COUNTY OF SAN MATEO

OFFICE OF THE SHERIFF

HALL OF JUSTICE AND RECORDS • REDWOOD CITY, CALIF.

EMERSON B-3911

ADDRESS ALL COMMUNICATIONS TO THE SHERIFF

EARL B. WHITMORE

SHERIFF

WESLEY A. POMEROY

UNDERSHERIFF

WILLIAM H. BLASER

CHIEF CIVIL DEPUTY

IDENTIFICATION OF PHENYLCYCLOHEXYLPIPERIDINE

(ALSO KNOWN AS PCP OR "PEACE PILLS")

I. PHYSICAL PROPERTIES

- A. Fine white powder packaged in bindles or capsules
- B. Ultraviolet absorption: 0.2N HCl
 - 1. Maximum - 262 (251.5) (257.5) (268.5)
 - 2. Minimum - 258.5 (253) 266.5)
- C. Appears to give extensive absorption in the infra red region of the electromagnetic spectrum

II. IDENTIFICATION TESTS

- A. All the classic field screening tests are negative except Wagner's reagent
- B. Microchemical crystal tests:
 - 1. Picric acid (see figure 1) with test material dissolved in weak sulfuric acid
 - 2. Potassium iodoplatinate reagent (see figure 2) is applied to weak acid solution of the material.
 - 3. Gold chloride reagent (see figure 3) is applied to a weak acid solution of the material
 - 4. Wagner's reagent (see figure 4) is applied to a weak acid solution of the material
- C. Color test (for screening only)-Prepare a fresh saturated solution of citric acid in Acetic Anhydride. Place a small amount of the solid unknown or an alcoholic solution of the unknown in a test tube with the citric acid-Acetic Anhydride solution. Immerse in a boiling water bath for 3 to 5 minutes. A red to violet color indicates a positive response.

Note: Blank should be performed coincidental with unknown

BUREAU OF DRUG ABUSE CONTROL

NOTES ON
CLANDESTINE LABORATORIES

CAUTION: THIS DOCUMENT IS FOR CONFIDENTIAL USE FOR AUTHORIZED LAW
ENFORCEMENT OFFICERS AND OFFICIALS

IDENTIFICATION OF ILLICIT LABORATORIES
BY THE REAGENTS PRESENT

The following is a grouping of chemicals under the specific drugs in whose synthesis they are used. There are many chemicals such as solvents (ether, alcohol, chloroform etc.) and reducing agents (lithium aluminum hydride) that are utilized in the synthesis of many or all of the covered drugs. The only reagents included are those used specifically in the manufacture of a single drug or group of drugs. The presence of any of the following chemicals in an illicit laboratory is a strong indication that the drug under which it is listed is the one being synthesized.

LSD

Ergotamine tartrate
Lysergic acid
Nitrogen
Dimethylformamide
Sulfur trioxide
Acetonitrile
Trifluoroacetic anhydride
Diethylamine

Mescaline

3, 4, 5 trimethoxyphenylacetonitrile
3, 4, 5 trimethoxybenzoic acid
3, 4, 5 trimethoxybenzyl chloride
3, 4, 5 trimethoxybenzyl alcohol

DMT

Indole
Oxalyl Chloride
Tetrahydrofuran
Dimethylamine
Amphetamine Sulfate

Phenylacetone (phenyl 2 - propanone)
Formamide
Hydroxyl amine

Methamphetamine HCL

Phenylacetone (phenyl 2 - propanone)
Ephedrine
Zinc or tin foil

THE HALLUCINOGENS

LSD (d-lysergic acid N, N-diethyl amide)

In the methods usually employed in the illicit synthesis of LSD, lysergic acid is always one of the raw materials. Commerce in lysergic acid, however, is controlled so it is frequently synthesized illicitly. A method for the synthesis of lysergic acid which employs ergotamine tartrate as a precursor is therefore included.

Synthesis of Lysergic Acid

Materials: ergotamine tartrate; potassium hydroxide; methanol; ethanol; ethyl ether; isopropanol; concentrated sulfuric acid; nitrogen gas; ammonia gas

Apparatus: Vacuum pump; evaporator; balance; heating mantle; water bath; ice bath; condenser column; Buchner funnel; filter flask; graduated cylinder; congo red paper; filter paper; capillary dropping tubes; Florence flasks; assorted tubing and stoppers.

Synthesis of LSD

Method I

Materials: dimethylformamide; sulfur trioxide (Sulfon B); d-lysergic acid monohydrate; lithium hydroxide monohydrate; methanol; diethylamine; ethylene or methylene dichloride; saturated saline solution; ethyl ether; tartaric acid; nitrogen; drierite

Apparatus: 2 liter, 3 necked round bottomed flask; condenser column; drying tube; mechanical stirrer; dropping funnel; ice bath; balance; graduated cylinder; vacuum pump; evaporator; separatory funnels; additional flasks or beakers; pH paper or meter; assorted tubing and stoppers

Method II

Materials: d-lysergic acid; acetonitrile; trifluoroacetic anhydride; diethylamine; chloroform; benzene; basic alumina; anhydrous sodium sulfate; tartaric acid

Apparatus: balance; graduated cylinder ice bath; refrigeration unit (refrigerator freezer) or solid CO₂; condenser column; drying tube; vacuum pump; evaporator; separatory funnels; chromatograph column; flasks and beakers; pH paper or meter; assorted tubing and stoppers

Synthesis of Mescaline (3, 4, 5 trimethoxyphenethylamine)

Materials: 3, 4, 5 trimethoxyphenylacetonitrile; lithium aluminum hydride; anhydrous ether; concentrated sulfuric acid; ethanol; stick potassium hydroxide; concentrated sodium hydroxide solution

Apparatus: balance; graduated cylinder; ice bath; separatory funnels; Buchner funnel; filter flask; vacuum pump or forced water suction pump; ph paper or meter; filter paper; beakers; assorted tubing

Biochemical Production of Mescaline

Mescaline can be biochemically produced by cultivating the peyote cactus, *Lophophora Williamsii*, and extracting the alkaloid by the following process:

Materials: Peyote cactus; ethanol; ammonium hydroxide; chloroform; hydrochloric acid; sodium carbonate; sodium hydroxide; sulfuric acid

Apparatus: balance; graduated cylinder; blender; Soxhlet extractor; heating mantle; Buchner funnel; filter flask; separatory funnels; titration burette; flasks and beakers; filter paper; ph paper or meter

Synthesis of D M T (N, N-dimethyl tryptamine)

Materials: dry tetrahydrofuran; indole; oxalyl chloride; dimethylamines; anhydrous ethyl ether; lithium aluminum hydride ($LiAlH_4$); benzene; methanol; technical ethyl ether; petroleum ether; sodium sulfate (anhydrous); chloroform: ~~anhydrous~~

Apparatus: 2000ml flask; 8.5cm Buchner funnel; filter flask and trap; vacuum source (a forced-water suction pump is least expensive); 800ml flask; 100ml graduated cylinder; capillary dropping tubes; ice bath; water bath; filter paper; additional flasks or glasses; rubber tubing; spatula or spoon; corks

Psilocybin

Psilocybin is the metabolizable form of dimethylhptamine. After injection it is broken down by the body to psilocin. Both psilocybin and psilocin can be chemically synthesized, however, during the synthesis DMT is produced first and from this the psilocybin is synthesized. This requires quite a bit of additional work, so it would be logical for most illicit operators to stop the process when they have isolated the DMT, or, if the desired product is psilocybin, to produce it biochemically. Procedures for the chemical synthesis of psilocybin and psilocin were developed by Hoffman, et al "Helvetica Chimica Acta" 42, 1570 (1959)

Biochemical Production of Psilocybin

Materials: potatoes; agar; dextrose; yeast extract; pure culture of *Psilocybe mexicana* or *Psilocybe cubensis*; methanol; distilled water

Apparatus: Five 1 pint fruit jars; two 2 liter beakers; balance; autoclave or pressure cooker; drying oven; inoculating loop; flannel or cheesecloth; heavy gauge aluminum foil

THE STIMULANTS

Synthesis of Amphetamine Sulfate

Method I

Materials: phenylacetone (phenyl 2 propanone); hydroxyl amine; methanol; hydrogen; sodium acetate; palladium black; potassium hydroxide; ether; sulfuric acid

Apparatus: Condenser column; heating mantle; ice bath; Buchner funnel; filter flask; vacuum pump; pressure reaction apparatus; separatory funnels; titration burette; balance; graduated cylinder; ph paper or meter; filter paper; clasks; assorted tubing and stoppers

Synthesis of Amphetamine Sulfate

Method II

Materials: phenylacetone; hydroxyl amine; methanol; lithium aluminum hydride; sodium acetate; potassium hydroxide; ether; sulfuric acid

Apparatus: Condenser column; heating mantle; ice bath; Buchner funnel; filter flask; vacuum pump; separatory funnels; titration burette; balance; graduated cylinder; ph paper or meter; filter paper; flasks; assorted tubing and stoppers

Synthesis of Amphetamine Sulfate

Method III

Materials: phenylacetone; formamide; ether; sulfuric acid

Apparatus: Condenser column; heating mantle; ice bath; vacuum pump; separatory funnels; titration burette; balance; graduated cylinder; ph paper or meter; flasks; assorted tubing and stoppers

Synthesis of Methamphetamine HCL

Method I

Materials: phenylacetone; methylamine; methanol; sodium acetate; hydrogen; palladium black; potassium hydroxide; ether; hydrochloric acid

Apparatus: Condenser column; heating mantle; ice bath; Buchner funnel; filter flask; vacuum pump; pressure reaction apparatus; separatory funnels; titration burette; balance; graduated cylinder; ph paper or meter; filter paper; flasks; assorted tubing and stoppers

Synthesis of Methamphetamine HCL

Method II

Materials: phenylacetone; methyl amine; methanol; lithium aluminum hydride; sodium acetate; potassium hydroxide; ether; hydrochloric acid

Apparatus: Condenser column; heating mantle; ice bath; Buchner funnel; filter flask; vacuum pump; separatory funnels; titration burette; balance; graduated cylinder; ph paper or meter; filter paper; flasks; assorted tubing and stoppers

Synthesis of Methamphetamine HCL

Method III

Materials: ephedrine; hydrogen iodide; potassium hydroxide; ether; hydrochloric acid

Apparatus: Condenser column; heating mantle; Buchner funnel; filter flask; vacuum pump; separatory funnels; titration burette; balance; graduated cylinder; ph paper or meter; filter paper; flasks; assorted tubing and stoppers

Synthesis of Methamphetamine HCL

Method IV

Materials: ephedrine; hydrochloric acid; zinc or tin foil; ether; potassium hydroxide

Apparatus: Condenser column; heating mantle; Buchner funnel; filter flask; vacuum pump; separatory funnels; titration burette; balance; graduated cylinder; ph paper or meter; filter paper; flasks; assorted tubing and stoppers

Properties of Unusual Reagents

Acetonitrile (methyl cyanide) CH₃CN.

Properties: Colorless, limpid liquid; aromatic odor; poisonous; sp. gr. 0.783; m.p. - 41°C; b.p. 82°C. Soluble in water and alcohol.

Typical specifications: Sp. gr. 0.782-0.785 (20°C); boiling range 80-82°C; purity 99% (min).

Derivation: By heating acetamide with glacial acetic acid; from dimethyl sulfate and sodium cyanide.

Grades: Technical.

Containers: drums; tanks.

Uses: Organic synthesis of vitamin B pharmaceuticals and others; perfumes; extracts; denaturant; purification of a variety of chemicals; specialized solvent, especially for extractive distillation; crystallization medium; fiber synthesis.

Shipping regulations: Poison, Class B. Poison label.

N,N-dimethyl formamide (DMF) HCON(CH₃)₂.

Properties: Water-white liquid; non-corrosive; b.p. 152.8°C; m. p. - 61°C; refractive index (n_{25/D}) 1.4269; sp. gr. 0.953-0.954 (15.6/15/6°C). Flash point (Tag open cup) 153 F. Miscible with water and most organic solvents, and many inorganic liquids.

Containers: 55-gal drums; tank cars; tank trucks.

Uses: Solvent for vinyl resins and acetylene, butadiene, acid gases, inorganic salts, some petroleum components; dyestuffs, and pharmaceuticals; used in making "Orlon."

Hydroxylamine (oxammonium) NH₂OH. The free base is unstable.

Properties: Colorless crystals; decomposes when heated and explodes at 130°C. Soluble in alcohol, acids and cold water. Sp. gr. 1.227; m.p. 33°C; b.p. 70°C.

Derivation: By decomposing hydroxylamine hydrochloride or sulfate with a base and distilling in vacuo.

Method of purification: Redistillation.

Containers: Lead-lined steel drums.

Uses: Reducing agent; organic synthesis.

Shipping regulations: None.

1/ Condensed Chemical Dictionary, Sixth Edition, Reinhold Publishing Corp., New York.

Lithium Aluminum Hydride (LAH) LiAlH_4 .

Properties: Light porous white powder. sp. gr. 0.917 g/ml. Sometimes turns gray on standing. Stable in dry air at room temperature, but very sensitive to moisture, even that in ordinary air. Decomposes to lithium hydride, aluminum metal and hydrogen above 130°C without melting. Soluble in diethyl ether, tetrahydrofuran, dimethyl "Cellosolve." Slightly soluble in dibutyl ether. Insoluble or very slightly soluble in hydrocarbons and dioxane.

Preparation: Reaction of aluminum chloride with lithium hydride.

Containers: Glass bottles; polythene bags placed in metal cans, up to 6-gallon capacity; steel drums, fiber cans.

Uses: Reducing agent for over 60 different functional groups, especially for pharmaceutical, perfume, and fine organic chemicals; source of hydrogen; propellant; catalyst in polymerizations.

Hazards: Caution! Obtain detailed information on precautions before opening containers of this material. May ignite spontaneously on grinding or rubbing, or from static sparks. Fires must be controlled by smothering with powdered limestone. All ordinary extinguishers must not be used.

Shipping regulations: Flammable solid. Yellow label.

Oxalyl Chloride (ethanedioyl chloride) $(\text{COCl})_2$

Properties: Colorless liquid. If cooled to 12°C , solidifies to a white, crystalline mass. Gives off carbon monoxide on heating. Decomposed by water and alkaline solutions. Caution! Very toxic! Soluble in ether, benzene, chloroform.

Constants: B.p. 64°C ; m.p. -12°C ; sp. gr. 1.43.

Derivation: Interaction of oxalic acid and phosphorus pentachloride.

Grades: Technical.

Containers: Steel drums.

Uses: Military poison gas; chemical (chlorinating agent in organic synthesis).

Sulfur Trioxide (sulfuric anhydride) SO₃; (SO₃) n.

Properties: Exists in three solid modifications; alpha, m.p. 6^oC; beta, m.p. 32.5^oC; gamma, m.p. 16.8^oC. The alpha form appears to be the stable form but the solid transitions are commonly slow; a given sample may be a mixture of the various forms, and its m.p. not constant. The solids sublime easily. The gamma form boils at 45^oC. An explosive increase in vapor pressure occurs when the alpha form melts. The anhydride combines with water, forming sulfuric acid and evolving a large amount of heat. It is strongly corrosive and an active oxidizing agent. Will produce severe burns.

Containers: (Stabilized, liquid) 750-lb drums; tank cars.

Uses: Sulfonation of organic compounds.

Shipping regulations: Corrosive liquid.

White label. It is usually generated in the plant where it is to be used.

Tetrahydrofuran (THF) C₄H₈O.

Properties: Water-white liquid with ethereal odor; sp. gr. (20^oC) 0.888; refractive index (n_{20/D}) 1.4070; f.p. - 65 C; b.p. 66^oC; flash point (open cup) 5^oF. Soluble in water and organic solvents.

Derivation: From furfural, as an intermediate in the production of adiponitrile.

Containers: 7-lb (1 gal) containers; 35- and 375-lb drums; 29,000-lb tank cars.

Uses: Solvent for natural and synthetic resins, particularly vinyls, in topcoating solutions, polymer coating cellophane, protective coatings, adhesives, printing inks, etc. Useful reaction solvent, e.g., in Grignard reactions, LiAlH₄ reductions, and polymerizations. Versatile chemical intermediate and monomer.

Shipping regulations: Flammable liquid. Red label.

TABLETS AND TABLET MANUFACTURE

Composition of Tablets

In addition to the active ingredient, a tablet is composed of a number of inert materials. These materials include diluents, binders, lubricants, disintegrators and colors.

A diluent is an inert substance which is added to the active ingredient in order to increase its bulk. The average LSD tablet contains between one and two thousandths of a gram of LSD, hence it is obvious that another material must be added to make tableting possible. Diluents used for this purpose include dextrose, lactose, Mannitol, kaolin, di-calcium phosphate, calcium sulfate and sodium chloride.

A binder is a substance used to impart cohesive qualities to the powdered material. They insure the tablet remaining intact after compression and also improve the free flowing qualities of the substance to be tableted. The most common binders are starch, gelatin, molasses, ethylcellulose, lactose, various natural and synthetic gums, and sugars such as sucrose. Binders are used both as a solution and in dry form depending on the other ingredients in the formulation and the method of preparation.

The functions of a lubricant are the prevention of adhesion of the tablet material to the surface of the dies and punches, the improvement of the rate of flow of the tablet granulation, and the reduction of interparticle friction. Some examples of lubricants are talc, starch, magnesium stearate, calcium stearate, boric acid, paraffin, stearic acid, cocoa butter, soaps, and sodium chloride.

A disintegrator is a substance, or mixture of substances, added to a tablet to facilitate its breakup after administration. The most common disintegrators are corn and potatoe starch. Other disintegrators include methylcellulose, agar, bentonite, other cellulose and wood products, and mixtures of citric, tartaric, or other acids with carbonates or bicarbonates.

Colors serve to identify specific tablets as well as improve their appearance. Any of the water-soluble FD&C dyes may be used to color tablets.

The following is the composition of a typical LSD tablet:

LSD	0.025mg
Gum Arabic	0.100mg
Stearic Acid	0.600mg
Tartric Acid	1.000mg
Talc	2.500mg
Corn Starch	5.000mg
Mannitol	20.775mg
	<u>30.000mg</u>

The Tablet Machine

The basic mechanical unit in tablet compression involves the operation of two steel punches within a steel die cavity. The tablet is formed by the pressure exerted on the granulation by the punches within the die cavity, and assumes the shape of the punches and die used.

Tablet machines are of two basic types; the single punch and the rotary punch machines. Single punch machines are the simplest and generally the smallest. The majority of the single punch machines are power driven, however, several hand-operated models are available. The capacity of these machines varies from approximately 65 tablets per minute to about 130 tablets per minute. The single punch machine is the one most likely to be used by illicit tableters because it is smaller, quieter, less expensive, and easier to operate than the rotary machine.

The principle of operation of the rotary machine is the same as the single punch machine, however, instead of having one set of punches and dies, the rotary machine has a head carrying a number of sets of punches and dies which revolves continuously while the tablet granulation runs from the hopper into the dies placed in a large, steel plate revolving under it. The number of sets of punches and dies varies from about four to about 51, and the capacity varies from 300 to approximately 6000 tablets per minute.

Tablet Production

There are three basic methods of tablet preparation. These include wet-granulation, dry-granulation, and direct compression. The most widely used method is the wet-granulation method. In this method the active ingredient, diluent, and disintegrator are mixed or blended well. For small batches, this can be done in bowls, but for larger quantities and more uniform blending, a twin-shell blender should be used. These come in many sizes from laboratory models to large production models. After the powder mass is blended well, it is wetted while mixing with a solution of the binding agent and coloring agent until the mass has the consistency of brown sugar. The wet granulation is forced through a 6 or 8 mesh screen, placed on large sheets of paper on shallow trays, and placed in drying cabinets with a circulating air current. After drying the granulation is reduced in particle size by passing it through a smaller mesh screen. Following dry screening, the lubricant is added as a fine powder. It is usually screened into the granulation through 100-mesh nylon cloth, and then gently blended with the granulation in a blender. The granulated mixture is then poured into the hopper of the tableting machine and compressed into tablets.

The dry-granulation method consists of blending the active ingredient, the diluent, the coloring agent and part of the lubricant. Either the diluent or the active ingredient should also be a good binder. Lactose is often used as both a diluent and a binder. The powder mass is then poured into the hopper of the tableting machine and compressed into large tablets

(generally 7/8 to 1 inch) called "slugs". The compressed "slugs" are then forced through a screen and the remaining lubricant is screened into the granulation. The granulation is gently blended in a blender and then poured into the hopper of the tableting machine and compressed into the finished tablets.

The direct compression method of tablet preparation usually employs a forced-flow feeder which is designed to de-aerate light and bulky material. It maintains a steady flow of powder moving into the die cavities under moderate pressure and reduces air entrapment. With one of these devices working in conjunction with the tableting machine, it is only necessary to mix the tablet ingredients and compress the powder directly into tablets. It is possible to employ the direct compression method without a forced-flow feeder if the amount of active ingredient is small and a spray dried diluent is used. Both spray dried lactose and spray dried mannitol are commercially available.

The popularity of the wet-granulation method over the other two, even though it consists of a greater number of steps and requires more time and labor, is due to the increased probability that the granulation will meet all the physical requirements for the compression of good tablets.