

**Substance Abuse  
&  
Hazard Recognition in the Home:**

**A Special Presentation to  
Sacramento County Social Services**



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In Conjunction With:  
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Northern California Training Academy**

# Cannabinoids

# OBJECTIVE SIGNS AND SYMPTOMS OF CANNABIS METABOLITE INFLUENCE

## EYES:

HGN NOT PRESENT

VGN NOT PRESENT

STRABISMUS

DILATED PUPILS - REBOUND

REDDENED CONJUCTIVA

## PHYSICAL SIGNS:

DISTORTED RHOMBERG

LAUGHING

IMPAIRED DIVIDED ATTENTION

ELEVATED PULSE

## APPEARANCE:

DRY MOUTH

BODY TREMORS

## OTHER SIGNS:

EUPHORIA

RELAXED INHIBITIONS

FORGETFULNESS

DISORIENTATION

IMPAIRED DISTANCE/

DEPTH PERCEPTION

POSSIBLE ODOR OF

MARIJUANA

POSSIBLY PARANOID

RELAXED APPEARANCE

## IRIS CORNERSTONES:

PULSE ELEVATED

HGN NOT PRESENT

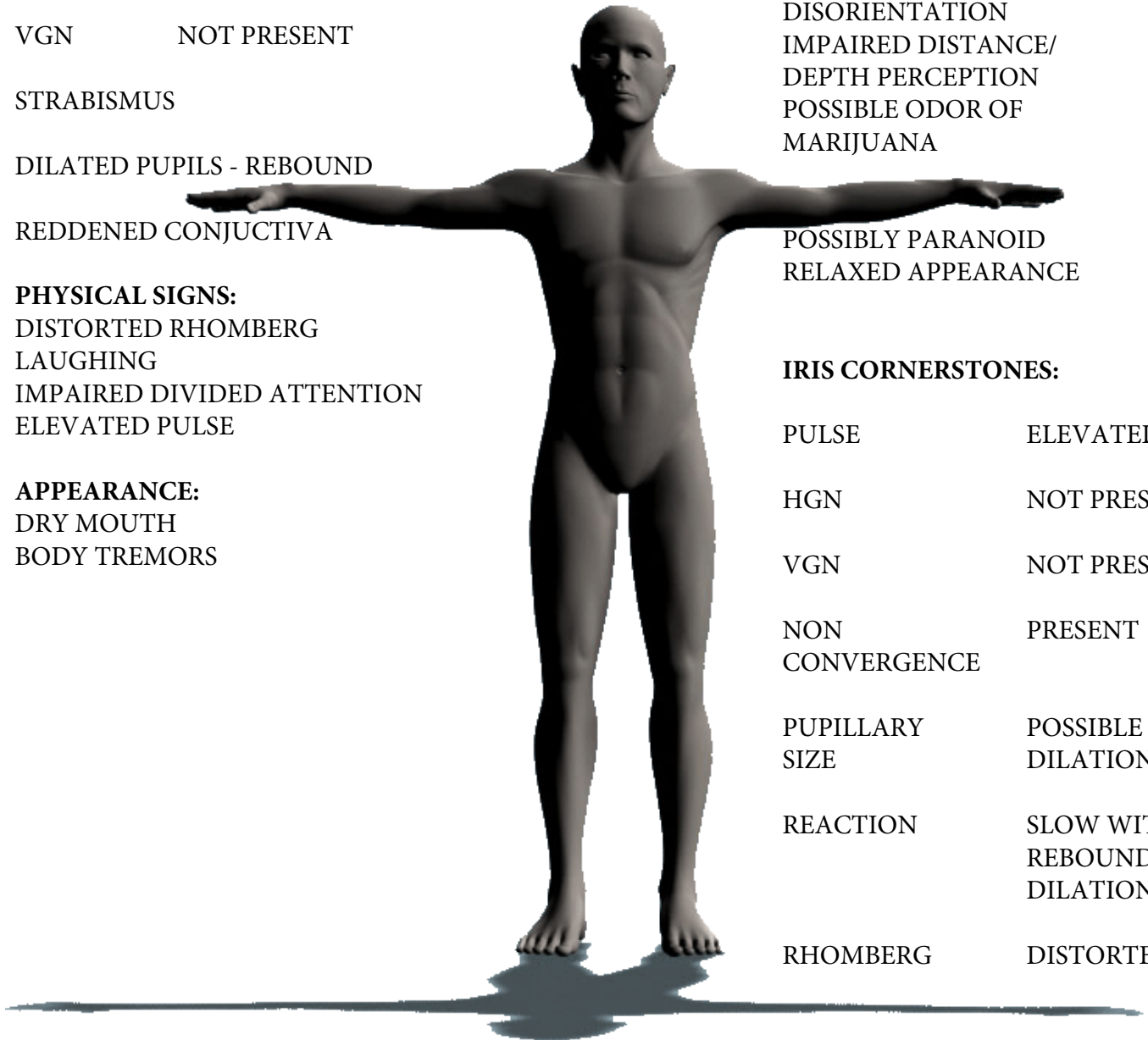
VGN NOT PRESENT

NON  
CONVERGENCE PRESENT

PUPILLARY  
SIZE POSSIBLE  
DILATION

REACTION SLOW WITH  
REBOUND  
DILATION

RHOMBERG DISTORTED





## **CANNABIS (MARIJUANA)**

CANNABIS IS THE CATEGORY OF DRUGS THAT ARE DERIVED FROM THE VARIOUS SPECIES OF CANNABIS PLANTS.

### **THE CANNABIS CATEGORY OF DRUGS INCLUDE:**

#### **MARIJUANA (SMOKED CANNABIS)**

##### **CONCENTRATED CANNABIS**

HASHISH

HASHISH OIL

##### **SYNTHETIC CANNABIS**

MARINOL

DRONABINOL

BOTH HASHISH AND HASHISH OIL ARE DERIVED FROM THE CANNABIS PLANT.

MARINOL IS A LEGALLY MANUFACTURED SYNTHETIC THC IN LIQUID FORM THAT IS PRESCRIBED FOR THE RELIEF OF NAUSEA ASSOCIATED WITH CHEMOTHERAPY.

ACTIVE COMPONENT IS:

#### **DELTA-9 TETRAHYDROCANNABINOL (THC).**

THIS PSYCHOACTIVE AGENT ASSOCIATED WITH THE CANNABIS PLANT IS CONCENTRATED IN THE RESIN (TRICHOMES) OF THE PLANT WITH THE MAJORITY OF THE RESIN FOUND IN THE FLOWERING TOPS OF THE FEMALE PLANT, WITH LESS FOUND IN THE LEAVES AND ALMOST NONE IN THE FIBROUS STALKS.

## **CANNABIS SYMPTOMATOLOGY:**

STIMULATION  
DECREASED ATTENTION SPAN  
MOOD ELEVATION  
EUPHORIA  
SEDATION  
GIDDY  
SLOW GAIT  
SLEEPY APPEARANCE  
MUSCLE RELAXATION  
ANESTHESIA  
INCREASED HEARING THRESHOLD  
MEMORY LOSS  
HALLUCINOGENIC  
HALLUCINATIONS  
PARANOIA DELUSIONS  
CRAVING FOR SWEETS  
POOR CONCENTRATION  
POOR MUSCLE COORDINATION  
POOR BALANCE  
SLOW SLURRED SPEECH  
PAIN RELIEF  
RED CONJUNCTIVA  
POOR DEPTH PERCEPTION  
TIME DISTORTION  
GLASSY EYES

### **CANNABIS PLANTS COME IN THREE SPECIES:**

#### **CANNABIS SATIVA L.:**

GROWN PRIMARILY IN MEXICO, COLOMBIA, JAMAICA AND THAILAND,

CANNABIS SATIVA HAS A RELATIVELY LOW THC CONTENT AND IS A SIXTEEN TO EIGHTEEN FOOT PLANT AT FULL MATURITY. IT IS SOMETIMES REFERRED TO AS "DITCHWEED" DUE TO ITS LOW THC CONTENT.

#### **CANNABIS INDICA:**

GROWN PRIMARILY IN THE MIDDLE EAST AND SOUTHEAST ASIA.

CANNABIS INDICA HAS A REDDISH



TINGE TO THE LEAVES, A RELATIVELY HIGH THC CONTENT AND IS A FIFTEEN FOOT BUSH AT FULL MATURITY. IT IS SOMETIMES REFERRED TO AS "SKUNK WEED" DUE TO ITS ODOR.

### **CANNABIS RUDERALISE:**

GROWN PRIMARILY IN RUSSIA, CANNABIS RUDERALISE HAS A RELATIVELY LOW THC CONTENT AND IS A TWO TO THREE FOOT PLANT AT FULL MATURITY.

IT HAS BECOME AVAILABLE IN THE UNITED STATES (VIA HIGH TIMES MAGAZINE ADVERTISERS WHO HAVE MADE THE SEEDS AVAILABLE VIA MAIL ORDER).

UNLIKE THE INDICA AND SATIVA STRAINS, THE RUDERALISE IS KNOWN AS "AUTO FLOWERING" WHICH MEANS THE FEMALE PLANT AUTOMATICALLY BEGINS TO "FLOWER" AFTER 6 WEEKS OF GROWTH.

### **SINSEMILLA:**

IS NOT A "SPECIES" OF CANNABIS, BUT OBTAINED AS A RESULT OF SPECIAL GROWING TECHNIQUES. SINSEMILLA PRODUCES THE HIGHEST THC CONTENT OF ANY OF THE GROWING TECHNIQUES. IT IS ESTIMATED THAT 95+% OF THE CANNABIS GROWN IN CALIFORNIA IS SINSEMILLA.

### **COMPARISON OF THC CONTENT:**

CANNABIS SATIVA L. .05-6% THC

CANNABIS INDICA 8 -10% THC

CANNABIS RUDERALISE .05-6% THC

AMERICAN HIGHBRED 8 -10% THC

SINSEMILLA 8 - 34% THC

HASHISH 8 - 10% THC (34%)

HASHISH OIL 20 - 60% THC (90%)

### **HASHISH:**

HASHISH IS OBTAINED BY REMOVING THE RESIN HEADS VIA A SCREEN OR WATER FILTRATION PROCESS (KEIF OR BUBBLE HASH). THE TRICHOMES ARE COMPRESSED INTO ANY SHAPE DESIRED. HASHISH CAN APPEAR AS BROWN, GREEN, RED OR BLACK.

MAJOR MANUFACTURERS OF HASHISH ARE LOCATED IN MOROCCO, MEXICO, THE MIDDLE EAST AND THE CARIBBEAN. DUE TO CALIFORNIA LAW, HASHISH IS USED AS "MEDICINE" AND IS BEING PRODUCED IN LARGE QUANTITIES.

### **HASHISH OIL:**

HASHISH OIL IS OBTAINED THROUGH THE SOLVENT EXTRACTION OF THE TRICHOMES FROM THE PLANT MATERIAL . THERE ARE NUMEROUS FLAMMABLE SOLVENTS THAT CAN BE USED. THE SOLVENT DISSOLVES THE RESIN HEADS CONTAINING THE THC FROM THE PLANT MATERIAL. THE SOLVENT EVAPORATES LEAVING JUST THE THC AND THE RESULTING OIL CAN BE MANIPULATED .

THIS OIL DOES NOT HAVE THE ODOR OF MARIJUANA BECAUSE IT IS ONLY THE RESIN FROM THE PLANT, NOT THE PLANT ITSELF.

THE MANUFACTURE OF HASH OIL IS ILLEGAL IN CALIFORNIA (THIS INCLUDES MEDICAL MARIJUANA CASES).

DEPENDING UPON THE VARIOUS TECHNIQUES EMPLOYED, HASH OIL IS REFFERED TO AS; DABS, BUDDER, OIL (710 - OIL UPSIDE DOWN) HONEYCOMB, VAC, WAX, ESSENTIALS, AND EXTRACTS.

#### **PHARMACOLOGY:**

MARIJUANA, HASH, AND HASH OIL ARE MOST COMMONLY SMOKED, ALTHOUGH THEY CAN BE INGESTED ORALLY.

#### **ONSET OF EFFECTS:**

##### **MARIJUANA**

SMOKED 4 TO 6 SECONDS

EATEN 20 TO 40 MINUTES

##### **HASH**

SMOKED 4 TO 6 SECONDS

EATEN 20 TO 40 MINUTES

##### **HASH OIL**

SMOKED 4 TO 6 SECONDS

#### **METABOLITES OF THC:**

ONCE IN THE BODY, THC PARTIALLY CHANGES INTO TWO OTHER COMPOUNDS (METABOLITES); HYDROXY (OH-THC) AND CARBOXY (C-THC).

OH -THC AND C - THC DO NOT CAUSE THE EUPHORIC EFFECTS THAT THC DOES.

THEY DO, HOWEVER, CAUSE VISUAL, MENTAL, AND MOTOR IMPAIRMENT. ALTHOUGH THE THC MAY DISSIPATE FROM THE BODY WITHIN 2-3 HOURS, OH-THC AND C-THC REMAIN IN THE BODY LONGER.

C-THC HAS BEEN SHOWN TO REMAIN WITHIN THE BODY AND CAUSE IMPAIRMENT FOR UP TO 6 DAYS.

#### **DURATION OF EFFECTS:**

THC	2-3 HOURS
OH-THC	4-6 HOURS
C-THC	3-6 DAYS

#### **EUPHORIA:**

THC	YES
OH-THC	MILD, IF ANY
C-THC	NO

#### **IMPAIRMENT:**

THC	YES
OH-THC	YES
C-THC	YES

IN ADDITION TO THE LENGTHY PLASMA LIFE, THC HAS BEEN SHOWN TO BE EXTREMELY "LIPID SOLUBLE". THIS MEANS THAT ALTHOUGH IT DISAPPEARS FROM THE BLOOD WITHIN HOURS, SOME THC GOES INTO THE FATTY TISSUE OF THE BODY WHERE IT IS STORED AND RELEASED OVER A LONG PERIOD OF TIME (UP TO 45 DAYS AFTER INGESTION).

CHRONIC USE OF HIGH QUANTITIES OF THC CAN DISPLACE SUFFICIENT NOREPINEPHRINE AND ENDORPHIN SO AS TO CAUSE ADDICTION AND TOLERANCE.

DUE TO THE HIGH LEVELS OF THC COMPOUNDS INFLUENCE RECOGNITION HAS BEEN OBSERVED BY THE AUTHOR 48 HOURS AFTER INGESTION.

## **SHORT TERM EFFECTS:**

BLOODSHOT EYES, ODOR OF BURNT MARIJUANA  
LOSS OF SENSE OF TIME AND SPACE  
DROOPY EYELIDS  
RESIDUE IN MOUTH (GREEN TONGUE)  
REDUCED ATTENTION SPAN  
IMPAIRED MEMORY, BODY TREMORS  
SLOW RESPONSES

## **CHRONIC EFFECTS:**

MOTIVATIONAL SYNDROME  
LOWER MALE HORMONE LEVELS  
LUNG, THROAT, MOUTH CANCER  
INTERFERENCE WITH PHYSICAL AND EMOTIONAL DEVELOPMENT, BIRTH DEFECTS

## **ADDICTION LIABILITY:**

REPRODUCIBLE TOLERANCE  
PHYSICAL DEPENDENCE

## **AFTER 21 DAYS OF HEAVY USE:**

ONSET 10 HOURS OF CESSATION  
PEAKS WITHIN 48 HOURS  
TERMINATES BY FIFTH DAY OF ABSTINENCE

## **DESCRIPTION OF W/D SYMPTOMS:**

AGITATION  
RESTLESSNESS  
IRRITABILITY  
DEPRESSION  
TREMOR  
NAUSEA  
ANOREXIA

## **CANNABINOID NEUROCHEMISTRY:**

THE FOLLOWING INFORMATION REGARDING CANNABINOID NEUROCHEMISTRY IS TAKEN FROM THE:

REPORT OF THE COUNCIL ON SCIENCE AND PUBLIC HEALTH CSAPH REPORT 3-I-09

### **CANNABINOIDS AND THE ENDOCANNABINOID SYSTEM**

IN 1964, DELTA-9-TETRAHYDROCANNABINOL (HEREAFTER REFERRED TO AS THC) WAS IDENTIFIED AS THE PRIMARY PSYCHOACTIVE CANNABINOID IN CANNABIS SATIVA AND SUCCESSFULLY SYNTHESIZED.

RECEPTORS IN THE BRAIN AND PERIPHERY THAT BIND THC (CANNABINOID RECEPTORS) WERE DISCOVERED IN THE EARLY 1990S, AND THE IDENTIFICATION OF ENDOGENOUS COMPOUNDS THAT ACT AT CANNABINOID RECEPTORS (ENDOCANNABINOIDS) SOON FOLLOWED.

### **CANNABIS SATIVA:**

THE PLANT CONTAINS OVER 400 CHEMICAL COMPOUNDS. THE MAIN PSYCHOACTIVE SUBSTANCE IS GENERALLY BELIEVED TO BE THC, BUT MORE THAN 60 OTHER CANNABINOIDS HAVE BEEN IDENTIFIED IN THE PLANT (PHYTOCANNABINOIDS) AND PYROLYSIS PRODUCTS.

CANNABINOIDS ARE CHEMICAL COMPOUNDS THAT ARE UNIQUE TO THE CANNABIS PLANT. DELTA-8-THC IS SIMILAR IN POTENCY TO THC, BUT IS PRESENT IN ONLY SMALL CONCENTRATIONS. CANNABINOL AND CANNABIDIOL ARE THE OTHER MAJOR CANNABINOIDS PRESENT. THE FORMER IS SLIGHTLY PSYCHOACTIVE, BUT NOT IN THE AMOUNTS DELIVERED BY SMOKING MARIJUANA. CANNABIDIOL IS



NOT PSYCHOACTIVE AND HAS DISTINCTIVE PROPERTIES.

THE AVERAGE CONTENT OF THC IN CANNABIS PLANTS IS HIGHLY VARIABLE DEPENDING ON THE STRAIN, CLIMATE, SOIL AND GROWING CONDITIONS, AND HANDLING AFTER HARVEST.

THC IS A RESINOUS WEAK ACID,  $PKA = 10.6$ , WITH A VERY HIGH LIPID SOLUBILITY AND VERY LOW AQUEOUS SOLUBILITY. IT BINDS TO GLASS, DIFFUSES INTO PLASTIC, AND IS PHOTO LABILE AND SUSCEPTIBLE TO HEAT, ACID, AND OXIDATION; THESE CHARACTERISTICS HAVE SERVED AS BARRIERS TO THE DEVELOPMENT OF TRADITIONAL PHARMACEUTICAL DOSAGE FORMS.

THE (-) ENANTIOMER IS UP TO 100 TIMES MORE POTENT THAN THE (+) ENANTIOMER DEPENDING ON THE PHARMACOLOGICAL TEST.

### **CANNABINOID RECEPTORS:**

TWO TYPES OF CANNABINOID RECEPTORS (CB1 AND CB2) HAVE BEEN CLEARLY IDENTIFIED AND BOTH ARE MEMBERS OF THE SUPERFAMILY OF G-PROTEIN-COUPLED RECEPTORS. THE CB1 RECEPTOR, FIRST CLONED IN 1990, IS MAINLY EXPRESSED IN THE BRAIN AND SPINAL CORD.

DISTRIBUTION IS HETEROGENEOUS WITH THE HIGHEST DENSITIES PRESENT IN THE BASAL GANGLIA, HIPPOCAMPUS, AND CEREBELLUM, WITH COMPARATIVELY FEWER RECEPTORS IN THE BRAINSTEM.

CB1 RECEPTORS ARE AMONG THE MOST ABUNDANT G-PROTEIN COUPLED RECEPTORS IN THE BRAIN. BY COUPLING PREDOMINATELY TO INHIBITORY G

PROTEINS, CB1 RECEPTORS INHIBIT CERTAIN INWARDLY DIRECTED CALCIUM

CHANNELS, ACTIVATE OUTWARDLY DIRECTED POTASSIUM CHANNELS, AND ACTIVATE VARIOUS MITOGEN-ACTIVATED PROTEIN (MAP) KINASES.

THE LATTER MAY PLAY A ROLE IN THE MODULATION OF SYNAPTIC PLASTICITY, CELL MIGRATION, AND NEURITE REMODELING.

CB1 RECEPTORS ARE LOCATED ON THE TERMINALS OF CENTRAL AND PERIPHERAL NEURONS. GENERALLY, THEIR ACTIVATION INHIBITS THE ONGOING RELEASE OF A NUMBER OF DIFFERENT EXCITATORY AND INHIBITORY TRANSMITTERS, OR HYPERPOLARIZES NEURONS, WHICH ALSO INHIBITS ACTIVITY.

THE CB2 RECEPTOR, FIRST CLONED IN 1993 IS PREDOMINANTLY EXPRESSED IN CELLS OF THE IMMUNE AND HEMATOPOIETIC SYSTEMS BUT ALSO IS PRESENT IN NONPARENCHYMAL CELLS OF THE LIVER, ENDOCRINE PANCREAS, AND BONE.

SOME CB2 RECEPTORS ALSO ARE FUNCTIONALLY EXPRESSED IN THE CNS, NOTABLY ON MICROGLIAL CELLS. CB2 RECEPTOR ACTIVATION ALTERS THE RELEASE OF CYTOKINES FROM IMMUNE CELLS AND PARTICIPATES IN THE REGULATION IMMUNE FUNCTION.

CB2 AGONISTS GENERALLY SUPPRESS THE FUNCTIONS OF THESE CELLS. CB2 MODULATES IMMUNE CELL MIGRATION BOTH WITHIN AND OUTSIDE THE CENTRAL NERVOUS SYSTEM

### **ENDOCANNABINOIDS:**

IN PARALLEL WITH THE DISCOVERY OF CANNABINOID RECEPTORS, ENDOGENOUS SUBSTANCES THAT BIND AND ACTIVATE THESE RECEPTORS WERE IDENTIFIED (ENDOCANNABINOIDS). THE TWO BEST CHARACTERIZED ARE ARACHIDONIC ETHANOAMIDE (AEA OR ANANDAMIDE) AND

2-ARACHIDONOYLGLYCEROL (2-AG), ALTHOUGH OTHER PUTATIVE ENDOCANNABINOIDS ALSO HAVE BEEN IDENTIFIED.

IN CONTRAST TO CONVENTIONAL NEUROTRANSMITTERS, ENDOCANNABINOIDS ARE NOT STORED IN SYNAPTIC VESICLES, BUT ARE PRODUCED ON DEMAND VIA CLEAVAGE OF MEMBRANE LIPID PRECURSORS AND THEN RELEASED AFTER DE NOVO SYNTHESIS.

ONCE FORMED IN RESPONSE TO PRESYNAPTIC DEPOLARIZATION, ENDOCANNABINOIDS FUNCTION AS “RETROGRADE” MESSENGERS, DIFFUSING BACK ACROSS THE SYNAPSE AND SIGNALING THE PRESYNAPTIC (UPSTREAM) NEURON TO DECREASE NEUROTRANSMITTER RELEASE AND/OR ACTIVITY.

THESE EFFECTS HAVE BEEN IMPLICATED IN THE MODULATION OF BOTH SHORT- AND LONG TERM SYNAPTIC PLASTICITY, EVENTS WHICH ARE INTEGRAL TO THE REMODELING OF SYNAPTIC NETWORKS IN THE CNS, AS WELL AS FUNDAMENTAL PROCESSES SUCH AS LEARNING AND MEMORY.

TERMINATION OF THE ACTION OF AEA AND 2-AG IS ACCOMPLISHED BY RE-UPTAKE INTO THE NEURON AND SUBSEQUENT ENZYMATIC DEGRADATION. THESE TRANSPORT PROTEINS AND DEGRADATIVE ENZYMES REPRESENT OTHER TARGETS FOR MANIPULATING THE ENDOCANNABINOID SYSTEM.

AEA PRIMARILY ACTIVATES CB1 RECEPTORS, AND ALSO STIMULATES TRPV1 RECEPTORS. THE LATTER IS AN IMPORTANT COMPONENT OF PAIN SIGNALING PATHWAYS. AEA IS A PARTIAL OR FULL AGONIST AT CB1 RECEPTORS, DEPENDING ON THE SPECIES, TISSUE,

AND BIOLOGICAL RESPONSE BEING

EXAMINED.

PARTIAL AGONISTS ARE CAPABLE OF BINDING TO A RECEPTOR, BUT DO NOT CAUSE MAXIMAL ACTIVATION. PHARMACOLOGICALLY, THEY CAN FUNCTION AS AGONISTS OR ANTAGONISTS, DEPENDING ON THE DOSE, AND ENDOGENOUS ACTIVITY OF THE BIOLOGICAL SYSTEM THEY ARE INTERACTING WITH. THIS FACT COMPLICATES THE INTERPRETATION OF ENDOCANNABINOID EFFECTS THAT HAVE BEEN OBSERVED IN ANIMAL MODELS, AS WELL AS FINDINGS WHICH MAY BE RELEVANT TO PHYTOCANNABINOIDS SUCH AS THC.

ALTHOUGH AEA BINDS TO CB2 RECEPTORS, IT HAS A LOW EFFICACY, AND MAY ACT PRIMARILY AS AN ANTAGONIST. 2-AG HAS APPROXIMATELY EQUIVALENT ACTIVITY AT CB1 AND CB2 RECEPTORS, IS MUCH MORE ABUNDANT THAN AEA IN THE BRAIN, AND IS BELIEVED TO ACT PRIMARILY AS AN AGONIST AT CANNABINOID RECEPTORS. OTHER PUTATIVE ENDOCANNABINOIDS ALSO TEND TO BE CONSIDERABLY MORE ACTIVE AS CB1 RECEPTOR AGONISTS. ADDITIONALLY, OTHER RECEPTOR SYSTEMS APPEAR TO RESPOND TO ENDOCANNABINOIDS.

THC IS ALSO A PARTIAL AGONIST AT THE CB1 AND CB2 RECEPTORS. CANNABIDIOL DISPLAYS ANTI-OXIDANT ACTIVITY, IS A TRPV1 AGONIST LIKE AEA, AND INHIBITS THE UPTAKE AND METABOLISM OF AEA. IT HAS LOW EFFICACY FOR CB1 AND CB2 RECEPTORS.

TAKEN TOGETHER, THE ENDOCANNABINOID SYSTEM IS WIDELY DISPERSED AND IT MODULATES THE ACTIVITY OF SEVERAL PROMINENT NEUROTRANSMITTERS, IMMUNE REGULATING CELLS, AND OTHER

TISSUE AND ORGANS. ACCORDINGLY,

ENDOCANNABINOIDS LIKELY PLAY A ROLE IN THE REGULATION OF A WIDE VARIETY OF FUNCTIONS AND DISEASE STATES. SOME OF THE MOST PROMINENT INCLUDE APPETITE REGULATION, PERIPHERAL ENERGY METABOLISM, OBESITY AND ASSOCIATED METABOLIC ABNORMALITIES, PAIN AND INFLAMMATION, GASTROINTESTINAL MOTILITY AND SECRETION, CENTRAL NERVOUS SYSTEM DISORDERS, NEUROTOXICITY/NEUROINFLAMMATION/NEUROPROTECTION, AND CERTAIN MENTAL DISORDERS, INCLUDING SUBSTANCE MISUSE.

## **BRIEF HISTORY OF CANNABIS AS A MEDICINE:**

THE FOLLOWING INFORMATION REGARDING CANNABIS AS A MEDICINE IS TAKEN FROM THE:

THE ROLE OF THE PHYSICIAN IN "MEDICAL" MARIJUANA, SEPTEMBER 2010

AMERICAN SOCIETY OF ADDICTION MEDICINE (ASAM)

## **MODERN HISTORY OF CANNABIS IN MEDICINE**

IN THE EARLY PART OF THE 19TH CENTURY, THE EUROPEAN MEDICAL COMMUNITY BECAME AWARE OF THE THERAPEUTIC POTENTIAL OF CANNABIS-BASED MEDICATIONS.

DR. WILLIAM O'SHAUGHNESSY, AN IRISH PHYSICIAN, CONDUCTED CLINICAL AND NONCLINICAL WORK IN INDIA WITH CANNABIS PREPARATIONS AND UPON HIS RETURN TO ENGLAND, THE RESULTS OF HIS STUDIES BECAME WIDELY KNOWN.

ACROSS EUROPE AND NORTH AMERICA INTEREST INCREASED IN THE THERAPEUTIC POTENTIAL OF THESE MATERIALS. (O'SHAUGHNESSY WB, 1973)

PHARMACISTS AND EARLY PHARMACEUTICAL COMPANIES DEVELOPED ORAL CANNABIS EXTRACTS AND TINCTURES FOR VARIOUS MEDICAL CONDITIONS (HAMILTON HC, LE-SCOHIER AW & PERKINS RA, 1913).

THESE CANNABIS PREPARATIONS WERE UNSTABLE AND UNRELIABLE, HOWEVER, BECAUSE UNLIKE OPIATES, CANNABINOIDS ARE LIPID-, RATHER THAN WATER-SOLUBLE, AND SENSITIVE TO DEGRADATION BY HEAT AND LIGHT (GARRETT ER, HUNT CA, 1974).



BECAUSE OF THESE CHARACTERISTICS, AND THE LIMITED TECHNOLOGY AVAILABLE AT THE TIME, THE ACTIVE INGREDIENTS IN CANNABIS PREPARATIONS WERE UNKNOWN, THE PREPARATIONS LACKED STANDARDIZATION, AND PATIENT RESPONSE WAS VARIABLE.

REPORTS OFTEN BLAME THE ENACTMENT OF THE FEDERAL MARIHUANA TAX ACT OF 1937, WHICH IMPOSED ADMINISTRATIVE LIMITATIONS ON THE PRESCRIPTION OF CANNABIS PREPARATIONS, FOR THE CONTRACTION IN THE USE OF MARIJUANA IN MEDICINE.

THE MAIN REASONS FOR THIS DISAPPEARANCE WERE THE VARIABLE POTENCY OF CANNABIS EXTRACTS, THE ERRATIC AND UNPREDICTABLE INDIVIDUAL RESPONSES, THE INTRODUCTION OF SYNTHETIC AND MORE STABLE PHARMACEUTICAL SUBSTITUTES SUCH AS ASPIRIN, CHLORAL HYDRATE AND BARBITURATES, AND THE RECOGNITION OF IMPORTANT ADVERSE EFFECTS SUCH AS ANXIETY AND COGNITIVE IMPAIRMENT (FANKHAUSER M, 2002).

ACCORDINGLY, CANNABIS PREPARATIONS GRADUALLY FELL OUT OF USE BY THE MEDICAL PROFESSION. AS ONE PROMINENT PHYSICIAN IN 1938 NOTED (WALTON RP,1938):

THE THERAPEUTIC APPLICATION OF CANNABIS IS MORE A MATTER OF HISTORY THAN OF PRESENT-DAY PRACTICE. SYNTHETIC ANALGESICS AND HYPNOTICS HAVE ALMOST ENTIRELY DISPLACED THESE PREPARATIONS FROM THEIR ORIGINAL FIELD OF APPLICATION. THE NEWER SYNTHETICS ARE MORE EFFECTIVE AND RELIABLE AND, IN ADDITION, HAVE BEEN MORE INTENSIVELY EXPLOITED BY COMMERCIAL INTERESTS.

THE DRUG HAS CERTAIN REMARKABLE PROPERTIES AND IF ITS CHEMICAL STRUCTURE WERE DETERMINED AND SYNTHETIC VARIATIONS DEVELOPED, SOME OF THESE MIGHT PROVE TO BE PARTICULARLY VALUABLE, BOTH AS THERAPEUTIC AGENTS AND AS EXPERIMENTAL TOOLS.

WALTON'S PREDICTIONS TODAY REMAIN BOTH HOPEFUL AND ELUSIVE. BECAUSE OF THE TECHNOLOGICAL CHALLENGES INVOLVED IN CANNABINOID FORMULATION AND RESEARCH, IT WAS NOT UNTIL 1964 THAT THE PRIMARY PSYCHOACTIVE INGREDIENT IN CANNABIS, DELTA-9-TETRAHYDROCANNABINOL (THC), WAS IDENTIFIED AND SYNTHESIZED (MECHOULAM R & GAONI Y, 1965).

COINCIDENTALLY, POPULAR INTEREST IN SMOKED CANNABIS BEGAN TO INCREASE SIGNIFICANTLY. A NUMBER OF INDIVIDUALS REPORTED THAT SMOKING CANNABIS FOR RECREATIONAL PURPOSES SEEMED TO ALLEVIATE SOME OF THEIR MEDICAL SYMPTOMS. INTEREST GREW IN FINDING THERAPEUTIC USES FOR SMOKED CANNABIS. MORE ADVANCED TECHNOLOGY IN THE 1800S AND EARLY 1900S MIGHT HAVE MADE A RANGE OF CANNABINOID MEDICATIONS SIMILAR TO THAT OF MODERN OPIATES AVAILABLE, AND CANNABIS SMOKING MIGHT HAVE BEEN RELEGATED TO THE REALM OF NON-DEPENDENT, NON-MEDICAL USE FOR PLEASURE (MCCARBERG WH & BARKIN RL, 2007). THUS, THE "LAG" IN THE TECHNOLOGICAL CAPABILITIES OF MODERN SCIENCE PROBABLY CONTRIBUTED TO THE CONTROVERSY OF "MEDICAL MARIJUANA." THAT TECHNOLOGY HAS NOW ARRIVED, AND THE ERA OF MODERN CANNABINOID MEDICATION DEVELOPMENT IS WELL ON ITS WAY.

## SYNTHETIC CANNABINOIDS (SC)

### WHAT ARE THEY?

DESIGNED TO MIMIC THC AND OTHER CANNABINOIDS

DEVELOPED TO RESEARCH CANNABINOID RECEPTORS IN THE BRAIN

CANNABINOIDS ACT BY BINDING TO C1 AND C2 RECEPTORS

### HOW DO WE KNOW IF THE CANNABINOID HAS POTENTIAL FOR ABUSE?

STRENGTH OF CANNABINOID MEASURED BY AFFINITY CONSTANT (K<sub>i</sub>)

DIFFERENT CANNABINOIDS HAVE DIFFERENT K<sub>i</sub> VALUES

THE LOWER THE K<sub>i</sub> VALUE, THE HIGHER THE AFFINITY

HIGH AFFINITY IS CONSIDERED K<sub>i</sub> < 100 nM

FOR THC THE K<sub>i</sub> IS 10.2 nM

Substance	K <sub>i</sub> Value (nM)
JWH-018	2.9
JWH-073	8.9
JWH-200	42
CP-47,497	9.54
HU-210	0.06
<b>Δ<sup>9</sup>-THC</b>	<b>10.2</b>
JWH-081	1.2

### HOW MANY SC'S ARE THERE?

STRUCTURALLY THERE ARE 7 DIFFERENT CLASSES OF SC'S:

NAPHTHOYLINDOLES  
NAPHTHYLMETHYLINDOLES  
NAPHTHOYLPYRROLES  
NAPHTHYLMETHYLINDENES  
PHENYLACETYLINDOLES  
CYCLOHEXYPHENOLS  
CLASSICAL CANNABINOIDS

EACH OF THESE CLASSES HAVE A MULTITUDE OF COMPOUNDS WITHIN THEM.

EACH OF THESE INDIVIDUAL COMPOUNDS ARE IDENTIFIED BY THE MANUFACTURER OF THE COMPOUND. THE FOLLOWING IS THE LIST OF THE ORIGINAL MANUFACTURERS

HU – HEBREW UNIVERSITY

JWH – DR. JOHN W. HUFFMAN

CP – CYCLOHEXYLPHENOLS  
DEVELOPED BY PFIZER

WIN – STERLING-WINTHROP  
PHARMACEUTICALS

RCS - RESEARCH CHEMICAL  
SUPPLIER (CHINA)

AM - ALEXANDROS MAKRIYANNIS

ALTHOUGH THESE COMPOUNDS ORIGINATED FROM THESE PERSON'S / LOCATIONS, A MAJORITY OF THESE COMPOUNDS ARE PRODUCED AND SOLD FROM CHINA.

## GENERAL CHARACTERISTICS:

LIPID SOLUBLE  
NON-POLAR  
FAIRLY VOLATILE  
MORE POTENT THEN DELTA9-THC  
AVERAGE DOSE IS < 1 MG.

SYNTHETIC CANNABINOIDS VARY IN  
POTENCY

## PRODUCTS MARKETING ON THE STREET:

SOLD AS HERBAL INCENSE

MARKETING SINCE 2002

DIFFERENT FLAVORS AVAILABLE

WHEN SMOKED – PRODUCES  
CANNABIS - LIKE EFFECTS

REPORTED TO CONTAIN A VARIETY  
OF SYNTHETIC CANNABINOIDS

THE EFFECTS PRODUCED BY EACH  
PRODUCT ARE NOT CONSISTENT

MARKETING AS HERBAL INCENSE  
“NOT FOR HUMAN CONSUMPTION”  
TO AVOID FDA CONTROL.

MOST ARE NOT SCHEDULED UNDER  
THE CONTROLLED SUBSTANCES  
ACT (CSA)

## FEDERAL REGULATIONS:

NOVEMBER 24, 2010

DEA IS USING ITS EMERGENCY  
SCHEDULING AUTHORITY TO  
TEMPORARILY CONTROL

JWH-018  
JWH-073  
JWH-200  
CP-47,497  
CANNABICYCLOHEXANOL

## DESIGNATED AS SCHEDULE I

HERBAL INCENSE PRODUCERS ALREADY  
REPLACING SYNTHETIC CANNABINOIDS  
WITH NEW ONES:

Product	K <sub>i</sub> Value (nM)
AM-694	0.08
AM-2201	1.0
RCS-4	?
JWH-122	0.69
JWH-210	0.46
WIN-48,098	?

## ISSUES OF SC'S:

DUI DRIVERS ARE IMPAIRED

DRUG SCREEN (-)

LAB NEEDS A SPECIFIC REQUEST TO  
DETECT

## OTHERS WHO ABUSE

PAROLEES

PROBATIONERS

WORKERS (WHO ARE DRUG TESTED)

MILITARY

COLOR TEST

(DUQUENOIS-LEVINE) –NEGATIVE

URINE SCREENING – NEGATIVE

CANINES WILL NOT DETECT





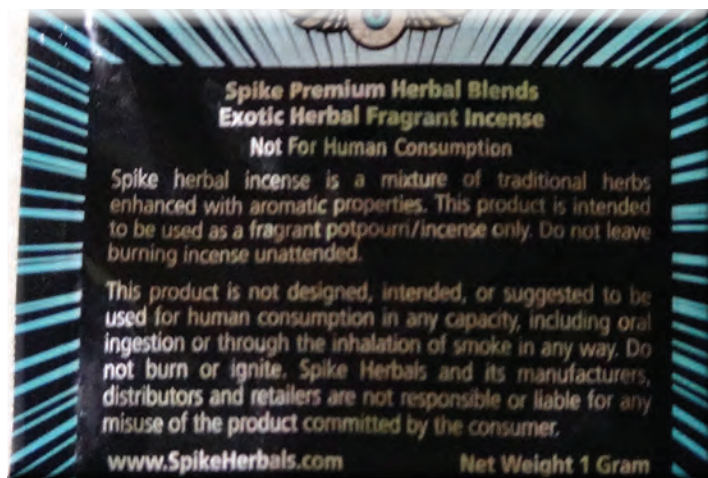
## Press Information Release:

### Designer Drugs From “Bath Salts” to “Spice”; What They Are, What They Look Like, And Why They Are Dangerous To Consume.

Edited and Released for Media by the Staff of New Leaf Treatment Center, Lafayette, CA  
S.Alex Stalcup, M.D. and Jackie Long, Director of Training

The Staff of New Leaf Treatment Center have received several inquiries from parents regarding the use of substances that are being sold as “Legal Highs” (also known as “Bath Salts” and “Spice”) by their children. Patients of New Leaf have also provided information regarding the prevalence and use of these compounds in the East Bay and Northern California area.

This press information release is being provided to dispel the myths of these “legal highs”, and to provide factual information as to the dangers and illegal use of these classes of designer drugs.



### **Synthetic Cannabinoids: What Are They And Are They Harmful?**

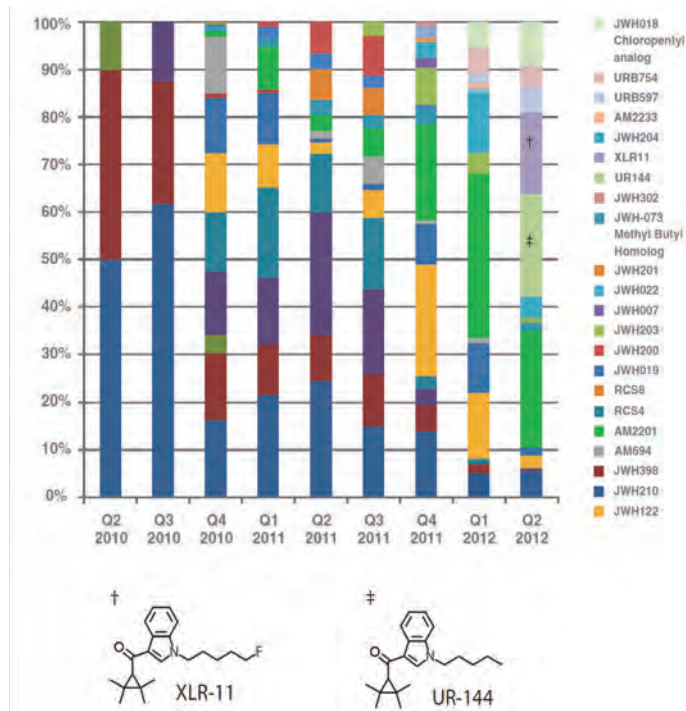
Often referred to as “Legal Weed”, synthetic cannabinoids (syn cannas) are classes of chemicals that activate the same pleasure pathways in the brain as the psychoactive chemical delta-9-Tetrahydrocannabinol

(THC) which is found in marijuana (cannabis). For a drug to have an effect on the human brain there has to be neurochemistry that is either activated or imitated by the drug. In the early 1990's the brain's natural (THC) neurotransmitter was identified and called Anandamide. This discovery allowed for continued research on the receptors found in the brain and body that are affected by cannabinoids (CB1 and CB2).

As a result of this research, 7 classes of syn cannas were developed (one internet site advertises 386 different syn cannas that it sells for “research”). Some of these compounds are many times (up to one hundred times) more potent than THC from cannabis. Syn cannas fully affect the CB1 receptor where THC only partially affects the CB1 receptor. It is important to note that none of these compounds were intended for human use or consumption.

In the August 2012 report from NMS Labs, it

documented that there were three primary syn cannas that were able to be identified in 2010. By 2012, that number had grown to thirteen. With the increasing research conducted by NMS Labs, additional syn cannas are being identified, and in 2012, additional syn cannas that have never been developed before were identified. (6)



Courtesy NMS Labs: Leading Bath  
Salt Compounds, June 2012

The terms “spice”, “incense”, or “herbal blends” is used when synthetic cannabinoid compounds are sprayed or soaked onto plant material (to resemble cannabis) and consumed by smoking. Currently there are new products that are being advertised and are sold in powder, capsule, and liquid form. (6) These compounds are sold under multiple different names (K-2, Spike, Spice, are just a couple of common names).



The same “loop hole” in the law exists for synthetic cannabinoids. The majority of these compounds are not regulated by law and as long as the package is marketed as “Not for Human Consumption” it is not regulated by the FDA. These products are being sold containing a form plant material that has been adulterated by not only one syn cann compound, but as many as five different syn cannas in an effort to “boost” the high.



Because these compounds activate the same brain chemistry as THC, the users are expecting the same euphoric effects as they would receive by consuming (smoking) cannabis. Unfortunately these syn cannas were not intended for human consumption and never studied to be consumed in combinations with other syn cannas. As a result, the consumption of these marketed compounds is very dangerous. Adverse reactions to the consumption of syn cannas include (7);

- Agitation,
- Alteration of time perception,
- Anxiety,
- Dysphoria,
- Elevated blood pressure,
- Listlessness
- Hallucinations,
- Nausea,
- Paranoia,
- Seizures,
- Tachycardia,
- Chest pain



Long term use of these compounds has been attributed to the loss of cognitive effects, halting of speech, avoidant eye contact, loss of consciousness, and confusion. It must be stressed that there is growing research that links the consumption (smoking) of these compounds to extreme anxiety, sudden depression, paranoia and hallucinations as being linked to the withdrawal of these compounds. There have been confirmed reports of deaths that have been attributed to the consumption of these compounds. In one case an adolescent died of coronary ischemia (not enough blood in the coronary arteries) and in another an adolescent committed suicide due to extreme anxiety from the drug. (8)

Mental health issues (psychosis) have also been attributed to the use of these compounds. In a report from a Central California Juvenile Probation Office, three adolescents on probation had to be admitted to a psychiatric ward for up to ten days after having an adverse reaction to smoking these compounds.

## Are These Compounds Legal In California?

In California some of these compounds are in a “grey area”. The majority of these compounds are not specifically identified as a controlled substance in the California Health & Safety (H&S) Code. There is an H&S section that makes a legal argument that these compounds can be illegal in California; The Controlled Substance Analog Act, 11401 H&S. (9)

This Act was passed by the California Legislature in 1988 in an effort to deal with the increasing designer drugs that were being formulated to bypass California law. Until this law was passed, if a substance was made that was not specifically listed in the H&S it was considered legal.

This law specifically states;

(c) the term “controlled substance analog” means either of the following:

(1) A substance the chemical structure of which is substantially similar to the chemical structure of a controlled substance classified in Section 11054 and 11055.

(2) A substance which has, is represented as having, or is intended to have a stimulant, depressant, or hallucinogenic effect on the central nervous system that is substantially similar to, or greater than, the stimulant, depressant, or hallucinogenic effect on the central nervous system of a controlled substance classified in Section 11054 or 11055.

Sections 11054 and 11055 of the Health and Safety Code are the first two “Schedules” of drugs that are controlled in California (11054 through 11058). These are referred to as Schedule I (not medically accepted) and Schedule II drugs (medically accepted).

In Schedule I, many hallucinogens, THC (along with its synthetic equivalents) and the stimulant hallucinogen MDA (MDMA-Ecstasy is an analog of MDA) are controlled. In Schedule II, methamphetamine, cocaine, and cathinone are controlled.

If the “bath salts” are identified to contain cathinone or methcathinone analogs they can be argued as a Schedule II controlled substance under H&S 11401. The syn cannas in “Spice” can be argued as analogs of Schedule I as a synthetic equivalent of THC. It should be noted that the filing of these compounds in a criminal court must be done so with prior consultation with the local District Attorney.

Currently there is a California law, H&S 11357.5, that makes it a misdemeanor to;

Sell, distribute, furnish, administer, give, offer to sell, any synthetic cannabinoid.

But the identified syn cannas in this act are; JWH 018, 73,200, CP47,497 and C8 homologue. These specific syn cannas are federally controlled, but in California it is only illegal to sell them; not to possess or use them.

What makes this a difficult law to enforce in California is that until the material is analyzed it is impossible to identify if it is illegal. Also as these compounds follow the federal law of 2010, these compounds have now been substituted for many other syn cannas that



are not regulated.

In July, 2012, a federal law, The FDA Safety & Innovation Act, Public Law 112-144 (S.3187), was passed which made certain syn cannns and certain compounds found in bath salts as controlled Schedule I compounds (banning sales, use, and possession). There are fi een syn cannns, Mephedrone, MDPV, and nine 2C compounds that are federally controlled. (10) As a federal law, it can only be enforced by federal agents in California as this law is not prosecutable in state court.

In California, the Drug Dealer Liability Act (H&S 11700-11717) may be a civil remedy for families that have suffered a loss by the use of these compounds. It is highly recommended that a before such an action is filed in Court, that consultation with a qualifi d attorney licensed to practice in California be conducted. New Leaf Treatment Center has staff available for consultation with legal professionals regarding the possible qualifi ations of designer compounds under this legal proceeding.

## **How Can I Recognize If Someone Is Using These Compounds?**

Aside from the identifi d symptoms of these compounds as described above, the recognition of influence of these compounds can be detected by law enforcement personnel and others who are trained in the Drug Abuse Recognition (DAR) or the Drug Recognition Expert (DRE) programs.

These compounds are designed to produce the same effect as controlled substances, they affect the same neurochemistry, thus influence is identifiable. As bath salts affect the same pathways of stimulants and hallucinogens, influence symptoms may include (depending on the dose consumed);

- Dilated pupils  
(Pupils that appear large and non-reacting in room or bright lighting conditions)
- Sweaty appearance
- Flushed appearance
- Clenching of the teeth
- Elevated body temperature
- Elevated pulse rate
- Talkative
- Muscle tremors or spasm



Influence Symptomatology

Synthetic Cannabinoids affect CB1 receptors in the brain (the receptor identifi d as causing the euphoria associated with THC in cannabis). Influence symptoms of syn cannns will mimic that of THC;

- Dilated pupils  
(Pupils that appear large in room and bright light conditions yet have a rebound under direct light)
- Elevated body temperature
- Elevated pulse rate
- Elevated body temperature
- Relaxed, droopy eye lids
- Non-convergence of the eyes



Normal Range Pupils



Constricted Pupils



Dilated Pupils

It must be stressed that one of the advantages and reasons for taking these compounds is that the majority of them are not detectable under normal urine and blood testing protocols. There are a few tests kits available on the market that claims they can test for “bath salts” and “Spice”. Caution is advised before using these test kits. Before purchasing or using these kits, confirm what specific designer compound the test will identify. Many will confirm for synthetics that are no longer being used due to their legal status, thus others will not be detected and provide a false “negative”. Please remember that “bath salts” and “spice” are only marketed names, not the real identity of the multitude of synthetic or other compounds that may be contained in the product.

NMS Labs has taken the lead in conducting research in the detection of these compounds on material and in urine and blood samples. As of this time NMS Laboratories does not provide a test kit for the open market, but NMS does have a program that is available to law enforcement and the medical community to provide analysis services. Refer to Reference Section for the contact information of

NMS Laboratories.

## If I Think There Is A Problem, Who Can Help Me?

There is mounting evidence to support that these compounds can produce addiction, physical dependency and withdrawal. New Leaf Treatment Center can provide outpatient services to assist in the medical treatment for addiction and withdrawal of these and other compounds. Local treatment providers may also have the same expertise and staff to render assistance, but it is suggested that their experience in treating these compounds is confirmed prior to utilizing their services.

In cases where the paraphernalia (including the packaging materials) is discovered and an intervention or assessment is needed, many law enforcement and public health agencies have the ability to assist. New Leaf Treatment Services also provides training programs regarding these compounds (drug trends and user identification) for law enforcement, public health, emergency services, social services, community organizations and parents.

In cases of an emergency, dial 911 and request assistance. In some cases law enforcement may be necessary to assist in dealing with the person who has become combative due to the acute intoxication from the drug. Medical services need to be watchful for the medical complications associated with excited delirium and be prepared for sedation and hyperthermia control. If the packaging of the material is found or available this should be given to the responding emergency personnel for possible analysis in the aid to treatment.

In cases of suspected depression by these compounds, seek medical assistance immediately. These instances may be immediate after the drug or may manifest days afterward. This depression can be treated, but if not addressed, it has led to documented suicides.

## Conclusion:

The belief that “bath salts” and “spice” products are “safe” due to their perceived “legal” status are placing

many users, their families, and their communities in danger. Serious mental and physical health issues are being reported by the wide spread use of these compounds. The medical staff, associate staff and training staff of NLTC are committed to addressing these issues in providing medical assisted treatment services for addiction and withdrawal of these and other compounds. NLTC is also committed to providing prevention, intervention, and treatment training services to law enforcement, court personnel, emergency services, public health, social services, schools and community services regarding these and other substances of abuse.

#### Special Thanks:

A special thank you to Dr. Logan and the staff from NMS Labs for allowing the use of their materials for this documentation.

#### Reference Contacts;

New Leaf Treatment Center, Dr. S. Alex Stalcup, Medical Director, 251 Lafayette Circle, Suite 150, Lafayette, CA 94549. Telephone 1 (925) 284-5200. Web: [www.nltc.com](http://www.nltc.com)

NMS Laboratories, 3701 Welsh Road, Willow Grove, PA 19090. Telephone: 1(800) 522-6671. Web: [www.nmslabs.com](http://www.nmslabs.com)

#### Material References;

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**CANNABIS SEEDS**



**CANNABIS SEEDS**



**SEEDLING**



**SEEDLINGS**



**VEGETATIVE  
STAGE**



**VEGETATIVE  
STAGE**





**YOUNG FEMALE  
FLOWERING**



**MALE PLANT  
POLLEN SACS (FLOWERS)**



**SINSEMILLA  
(WITHOUT SEEDS)**



**FEMALE PLANTS  
(FLOWERS)**



**HIGH GRADE  
SINSEMILLA**





**LOW GRADE CANNABIS  
(NOTE THE SEEDS)**



**MAGNIFIED PICTURE OF  
TRICHOMES (THC)**



**LOW GRADE CANNABIS  
PRESSED INTO CANS**



**TRIMMING OF BUD**



**BUDS CURING**



**BUDS**





**HARVESTED BUDS**



**CANNABIS LEAVES  
(SHAKE)**



**MAKING KEIF  
(HASHISH)**



**KEIF  
(HASHISH)**



**CANNABIS CIGARETTES  
(ROACHES)**



**CANNABIS CIGARETTES  
(ROACHES)**





**HAND ROLLED  
CANNABIS CIGARETTES**



**BLUNT WRAPS WITH BUD**



**COLLECTION OF EMPTY BLUNT WRAPS**



**TOBACCO EMPTIED FROM CIGARS  
FOR CANNABIS**



**CIGAR CUTTER**



**CIGAR CUTTER**

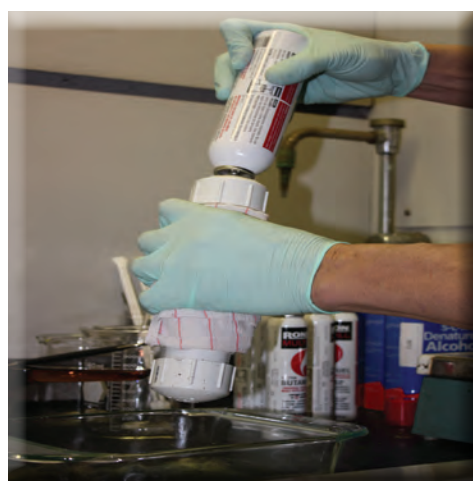




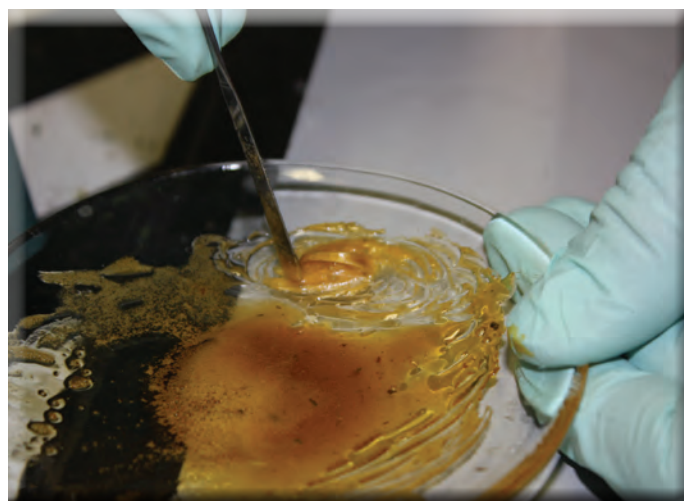
**BUTANE EXTRACTION LABORATORY**



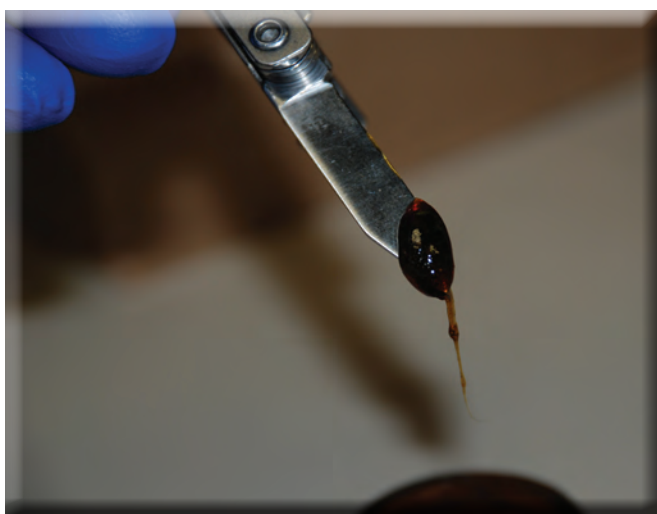
**EXTRACTION TUBE**



**EXTRACTING THC FROM  
CANNABIS MATERIAL**



**BUTANE "HONEY OIL"**



**BUTANE "HONEY OIL"**



**BUTANE "HONEY OIL"  
OR "DAB"**





**HONEY OIL OR DAB  
SMOKING MATERIALS**



**ELECTRONIC DAB SMOKING PEN**



**"BONGS"**



**PIPES**



**CLOSED PIPE**



**OPEN PIPE**





**CLOSED PIPE**



**OPEN PIPE**



**PIPES**



**PIPES**



**“GRINDERS”**



**“GRINDER”**





**BLUNT WRAPS**



**ROLLING PAPERS**



**“STASH” CANS**



**“STASH” CANS**



**“STASH” CANS**



**“STASH” CANS**





URINE KITS



URINE FLUSHES



HAIR DETOX



MOUTH DETOX



SMOKE FILTER



UNIVERSAL SIGN FOR CANNABIS USE



**“420 TIME”**



**SYNTHETIC CANNABIS  
“SPICE”**



**SYNTHETIC CANNABIS**



**CELL PHONE PICTURE FROM  
CANNABIS DEALER**



**“710” REPRESENTS CANNABIS  
OIL SMOKERS**



**“710” REPRESENTS CANNABIS  
OIL SMOKERS**

