Effect of Chronic Consumption of Cannabis Sativa Extract on Some Haematological Parameters in Wistar Rats

Sunday, Victor Ekuma, Olayi, Dominic Ogamode

College of Nursing and Midwifery Sciences, Moore Road, Calabar, Cross River, Nigeria

DOI: https://doi.org/10.51244/IJRSI.2025.12020096

Received: 05 February 2025; Accepted: 18 February 2025; Published: 25 March 2025

ABSTRACT

The use of cannabis also known as marijuana is often an under-reported activity in our society. Despite legal restriction, cannabis is still used by 10% - 15% of the world's population and chronic use could lead to psychotropic and physical adverse effects with a propensity for addiction. Population studies have also associated cannabis use with decreased pulmonary function, chronic obstructive airway diseases, and pulmonary infections.

However, smoking raw cannabis remains the most common and easiest route of intake but oral extract of cannabis has better evidence of relieving self-reported symptoms of spasticity caused by multiple sclerosis while the efficacy of smoked cannabis has been studied for Gilles de la Tourette syndrome, glaucoma, pain, with good evidence for clinical benefits in alleviating chronic and HIV-induced neuropathic pain.

In this study, fifteen (15) adult, male wistar rats, weighing 200-300g were used to test for the EFFECT OF CHRONIC CONSUMPTION OF CANNABIS SATIVA EXTRACT ON SOME HAEMATOLOGICAL PARAMETERS. The animals comprised of 3 groups i.e. control group and two test groups; the Low Dose (LD) and High Dose (HD) groups. All the animals in the two test groups (Low Dose and High Dose) daily received oral 1mg/100g body weight and 250mg/kg body weight of Cannabis *sativa* leaf extract for twenty-eight (28) days while the control group were fed with normal rat chow and water ad libitum without cannabis after an acclimatization period of seven (7) days, respectively. After 21 days, blood samples were obtained in all the animals by cardiac puncture technique for assessment of haematological parameters [Red Blood Cell Count (RBC), Haemoglobin Estimation (Hb), Packed Cell Volume (PCV) and Osmotic fragility].

It was observed that there was no significant decrease ($P<0.01$; $P<0.05$) in RBC Count of the HD group when compared with the LD and Control group, respectively. Haemoglobin concentration (Hb) and PCV were not significantly different in all groups while Osmotic fragility was seen to be statistically significant between the LD and HD groups when compared with the Control at 0.55 and 0.6 percentage NaCl Concentrations, respectively.

It can therefore be deduced that consumption of Cannabis *sativa* may be therapeutic but chronic consumption of it has effect on the body's defence mechanism that may lead to anaemia and reduced immunity.

INTRODUCTION

The use of cannabis also known as marijuana is often an under-reported activity in our society. Despite legal restriction, its use for either culinary, medicine or ceremonial purposes can be traced back to ancient cultures and still continues in our present society **(UNODC, 2008).** Though, the use of Cannabis as a psychoactive drug gave rise to its being nick named as "marijuana, pot, grass, weed, hemp, blow, puff, among many other names **(Amaza *et al.*, 2013).**

However, Cannabis *Sativa* is an old plant with a long history. It is an annual, herbaceaous and a dioecious plant that belongs to the specie of the *cannabaceae* family **(Adams and Martins, 1996).** It can grow up to 5 meters (8-12ft) tall when mature and the leaves are lanceolate on average 10cm (4 inches) length with serrated edges

ISSN No. 2321-2705 | DOI: 10.51244/IJRSI |Volume XII Issue II February 2025

that grow opposite each other on a stem which is frequently hollow and resinous **(Duke, 1983).** The plant is known to be a good source of food, industrial fibre, seed oil and is used for recreational, religious, medical and spiritual purposes. Each part of the plant is harvested differently depending on the purpose of its use **(Adams and Martins, 1996).**

There are two most abundant cannabinoids present in Cannabis. They are Δ9-Tetra-HydroCannabinol (THC), which creates the "high"(anxious effect), and Cannabidiol (CDB) which does not make one "high" but is found to have many therapeutic effects. In plants cultivated for drug use, there is more THC than CBD whereas the opposite is true for plants cultivated for fibre use. It is estimated that 50% of medicines in the last half of the 19th century were made from Cannabis hemp extract, high in CBD and Scientists believe that it is CBD that regulates the "high"(anxious) effect produced by THC **(Grégorio *et al.*, 2020).**

When Cannabis is grown to be consumed as a drug, it is the female plant that is used. The flower buds of the plant must remain unpollinated to ensure good THC production. It is these unpollinated flower buds that are then consumed by a user (i.e. either by smoking, vaporising, orally or intravenously. Extracting the oil/resin, cooking in butter to be used in food among many other uses are the other forms of ingestion. Other parts of the plant may be used to take full advantage of the psychotropic and therapeutic contents **(Grégorio *et al.*, 2020).**

According to **Morrison *et al.*, (2007)** marijuana is recognized as a substance with a high potential for dependence (occurring in 1 out of 10 people who have ever used cannabis). Though, [Endo-]cannabinoids are produced naturally in the bodies of humans and most animals but the effects of cannabis are brought on by naturally occurring chemicals known as [phyto-] cannabinoids. Moreover, Cannabis contains over 60 different [phyto-]cannabinoids and it's the only plant found so far to produce these chemicals **(Grégorio *et al.*, 2020).**

Cannabis is not as widely perceived as a harmless drug but poses significant potential physical and psychotropic side-effects and/or risks to the individual and the society. This is because Chronic usage of marijuana leads to behaviors of preoccupation, compulsion, reinforcement, withdrawal, incapacitation or death and negative impact on the quality of life of the user but clinical trials demonstrate benefits in alleviating chronic and neuropathic pain, treatment of glaucoma, relieve of depression and mitigation of nausea associated with the cancer treatment **(Leung, 2011)**. It's whole seeds are also good source of phosphorous, magnesium, zinc, copper, and manganese; in fact, hemp foods have no known allergies **(Amaza *et al.*, 2013)**.

It is to the above background that it became necessary to do further studies to ascertain whether the consumption of Cannabis *sativa* extract has effect on haematological parameters in wistar rats.

Background of the Study

Medicinal plants and some fruit trees have formed the basis of health care since the early days of humanity and have remained relevant for various chemotherapeutic purposes throughout the world. The use of plant derived natural compounds in addition to extracts from some fruits trees for alternate source of medication continues to play a major role in chemotherapy especially in third world countries like Nigeria. This is because plant and some fruits trees contain a variety of herbal and non-herbal ingredients that can ameliorate or trigger a disease condition by acting on a variety of targets (various modes and mechanism) in the host organism by means of secondary metabolism **(Akpaso *et al.*, 2011)**.

The **family:** *Cannabaceae* is one of the few herb plants that have attained popularity in laymen, amateur *collectors* as well as scholars. The **Genus:** Cannabis is a fast-growing bushy, annual plant with dense sticky flowers that produces the psychoactive Δ9-Tetra-HydroCannabinol (THC). It is the most widely used illegal psychoactive substance and has a long history of medicinal, recreational, and industrial use. The fibrous stalks of the plant are used to produce clothing and rope but that is usually in reference to hemp **(Grégorio *et al.*, 2020).** This herb plant and its products are consumed by many Nigerians and their counterparts all over the world where they are seen as being edible or as drug.

However, Blood is a connective tissue in fluid form. It is considered as the 'fluid of life' because it carries oxygen from lungs to all parts of the body and carbon dioxide from all parts of the body to the lungs. It is known as 'fluid of growth' because it carries nutritive substances from the digestive system and hormones from endocrine

ISSN No. 2321-2705 | DOI: 10.51244/IJRSI |Volume XII Issue II February 2025

gland to all the tissues. Blood is also called the 'fluid of health' because it protects the body against diseases and gets rid of the waste products and unwanted substances by transporting them to the excretory organs like kidney. More so, blood consists of the liquid portion known as "plasma" and blood cells which are called "formed elements". These blood cells are of three types; The Red blood cells (RBC) or erythrocytes, White Blood Cells (WBC) or Leucocytes and Platelets otherwise called thrombocytes **(Sembulingam and Sembulingam, 2012)**.

Blood carries out many functions in the body but these functions can be impaired by human actions and environmental agents. An example of this impaired function as a result of human action as confirmed by **Amaza *et al.*, (2013)**, is the varying degree of neurodegenerative changes seen in the cerebral cortex of albino rats administered with aqueous extract of cannabis *sativa*. They came up with the conclusion that consumption of cannabis *sativa* should be discouraged due to damage that may occur to the cells in the cerebral cortex.

Another example of impaired blood function as a result of human action as indicated by **Karimi *et al.*, (2007)** is the long term significant toxicological implication such as bone marrow suppression with respect to the concentration given on the erythrocytes of mammals. It was recommended that individuals who have anaemia or immunity complication should not use hemp seed in their food preparation on regular basis because hemp seed contains Δ9 tetrahydrocannabinols [THC] as its active constituents.

The most controversial use of Cannabis sativa is for its psychoactive and narcotic properties. This is because the plant may have effects on almost every system in the body, including the central nervous system, the heart, endocrine and immune systems **(Oseni *et al.*, 2006)**.

Aim and Objectives

There is quandary of information in literature regarding the effect of *Cannabis Sativa* consumption on most biochemical and physiological indices. Therefore, this article aims to update the current knowledge and evidence of using cannabis and its derivatives with a view to the socio-legal context and perspectives for future research.

However, this research work is embarked upon for the following reasons;

1. To determine the effect of *Cannabis sativa* consumption on blood.
2. To determine the effect of the test diet on the efficiency of the immune system.
3. To ascertain the effect of *Cannabis sativa* consumption on blood cell count.
4. To proffer advice of better edible substances that will be most beneficial to human health especially regarding blood.

Justification of Study

The use of Cannabis *sativa* has been documented to have systematic effects ranging from lowered testosterone secretion, impaired sperm production, motility and viability as well as disruption of ovarian cycle in females ***(*Ryan *et al.*, 2021*)***. Prolonged cannabis consumption is associated with blood flow interference which may lead to destruction of small vessels and eventual stroke **(BBC, 2012)**, while chronic Cannabis smoking is associated with bronchitis, emphysema and also has effects in the immune and endocrine systems **(Ashton, 2001)**.

It therefore became necessary to investigate its effect on haematological parameters since blood is a connective tissue to all the organs in the body.

LITERATURE REVIEW

Cannabis

According to the **World Health Organisation (1997),** Cannabis Locally called "Marihuana, Pot, Weed, Grass, Mary Jane, Bud and Ihgboo" is an annual herbaceous plant in the *Cannabis* genus. It's flowers are unisexual (i.e. only one sex is to be found on any one plant) and plants are most often either male or female. An explanation by Wikipedia (2017) further reveals that Cannabis (the most widely used illegal psychoactive) is the scientific name for a herb that produces a psychotropic cannabinoid called Tetra-hydrocannabinol (THC) along with an

ISSN No. 2321-2705 | DOI: 10.51244/IJRSI |Volume XII Issue II February 2025

array of cannabinoids. It is unique in that it is the only plant in the world to produce these chemicals that is usually produced in humans and animals **(Grégorio *et al.*, 2020)**.

Cannabis thrives on rich, fertile, neutral to slightly alkaline, well-drained silt or clay loams with moisture retentive sub-soils; it does not grow well on acid, sandy soils. The plant is reported to tolerate an annual precipitation range of 30 to 400cm, an average annual temperature range of 6-27°C and a pH in the range of 4.5 to 8.2. Its preferred name in other regions and countries include: hemp, English: marijuana, Spanish: canamo, sinsemilla. French: chanvre, Russian: konoplya, Arabic: hashish; kannab, Chinese: ma fen; ta ma. Portuguese: canhamo, Brazil: maconha, Germany: Hanf; Hungary: kender. India: charas; ganja. Italy: canapa. Japan: asa. Netherlands: hennep. Poland: kenop. South Africa: dagga; Sweden: hampa, Nigeria: ihgbo and many other names **(Plant for a future-PFAF, 2017)**.

Plant for a future-PFAF, (2017) further coined that many of the varieties and cultivars of cannabis have been selected for specific purposes as fibre, oil or narcotics and have been named as to the locality where it is mainly grown. More so, all so called varieties freely interbreed and produce various combinations of the characters. However, drug-producing selections grow better and produce more drugs in the tropics; oil and fibre producing specie thrive better in the temperate and subtropical areas while species grown in warmer climates tend to be best for medicinal use as those grown in more northerly latitudes produce the better fibre form of the plant with the yields of fibre varying according to climate and particular variety **(Plant for a future-PFAF, 2017)**.

The main psychoactive constituent of Cannabis is tetrahydrocannabinol (THC) but the plant is known to contain more than 500 compounds, among them are at least 113 cannabinoids; with most of them only produced in trace amounts. Aside from THC, another cannabinoid produced in high concentrations by some cannabis specie is cannabidiol (CBD), which is not psychoactive but has recently been shown to block the effect of THC in the nervous system. Differences in the chemical composition of *Cannabis* varieties may produce different effects in humans. Synthetic THC, called dronabinol, does not contain CBD, cannabinol (CBN), or other cannabinoids, which is one reason why its pharmacological effects may differ significantly from those of natural *Cannabis* preparations (**World Health Organisation – W.H.O, 1997)**.

More so, these natural compounds of the cannabis plant also referred to as phytocannabinoids of which Δ9-THC is the main psychoactive ingredient has been widely researched both in animals and humans. It characteristically produces, in a dose-dependent manner, hypo-activity, hypothermia, spatial and verbal short-term memory impairment. It is also believed to be primarily responsible for the resulting cognitive effects, psychotic symptoms, anxiety as well as the addictive potential of smoked cannabis **(Costa, 2007; Martin-Santos *et al.*, 2012)**. In 2010, the reported mean THC content of cannabis ranged from 1-12% for cannabis resin and from 1-16.5% for herbal cannabis **(EMCDDA, 2012)**.

However, the second major compound, CBD, does not affect loco-motor activity, body temperature or memory on its own but higher doses of CBD can potentiate the lower doses of Δ9-THC by enhancing the level of cannabinoid-1 receptor (CB1R) expression in the hippocampus and hypothalamus. This suggests that CBD potentiates the pharmacological effects of Δ9-THC via a CB1R-dependent mechanism **(Zerrin, 2012; Zuardi, 2012).**

Types of Cannabis

According to **Zambeza (2016),** there are thousands upon thousands of different cannabis strains, all with varying growing traits, tastes, aromas, yields and effects; but they all have something in common; they belong to one of the three families of cannabis –

1. Cannabis *ruderalis*
2. Cannabis *indica*
3. Cannabis *sativa*

Each of these names are used to describe three very different and unique sets of genetics found within the *Cannabaceae* family of plants (of which all cannabis varieties belong to), each with their own traits. Understanding the difference between these genetic families can help growers and researchers make an informed

ISSN No. 2321-2705 | DOI: 10.51244/IJRSI |Volume XII Issue II February 2025

decision about what they want to cultivate, and the preparations they will need to take to get the right marijuana **(Zambeza, 2016).**

The differences between these species of cannabis and their various effects on it's users as listed and explained by **Zambeza (2016),** include:

I. Cannabis *Ruderalis*: This is a relatively new line of cannabis within the cannabis cultivation scene. It can be found growing in the wilds of the colder regions of the world, usually above 50 degrees north of the equator (in such places as Russia and China). The main feature of the *ruderalis* family is that it is autoflowering (meaning the cultivator does not need to get involved), and can leave their marijuana crop largely to itself. *Ruderalis* strains are also very small and very fast growing. Wikipedia (2017), coined that Cannabis *ruderalis* is short, branchless, produce very small leaves, grows wild and is of no psychotropic value.

Effects:

- Cannabis *ruderalis* has very low levels of THC and CBD, making it have no effect and worthless to use in a pure form. What this means is that *ruderalis* does not really have any effects in itself, but its potential effect is reliant on the *sativa* or *indica* genetics it has been bred with. This is largely why they have not been utilized by the market up until recently.

- However, when bred with *sativa* or *indica* strains, it is possible to produce a *sativa* or *indica* dominant plant that retains the auto flowering features of the *ruderalis*. This is a huge advantage for many growers, especially those who live in colder areas of the world, and/or those who grow it outdoors. This implies that the crop can be planted, maintained with little effort and then replanted right after harvest.

II. Cannabis *Indica*: These plants are most commonly recognized by their short and stocky stature. This variety of cannabis originated in the wilds of sub-tropical countries, such as Pakistan and Afghanistan (which is sometimes reflected in a strain's name). Anywhere between 30-50 degree north and south of the equator tends to have the ideal climate for them. Because these are further away from the equator than their *sativa* cousins, the hours by which cannabis *indica* plants are exposed to daylight tend to fluctuate much more. This means that once the plants have reached their ideal height, they put all of their energy into producing flowers, utilizing the changing hours of day to the best of their ability.

Cannabis *indica* leaves grow much wider in order to utilize as much sunlight as possible. This urgency to take full advantage of the sun has resulted in a line of cannabis plants that flower much faster than their *sativa* counterpart. This combined with their much smaller stature makes *indica* strains extremely attractive to those who are growing for money – where space and speed directly relate into potential profit. Other unique features of Cannabis *indica* is that it has a higher level of CBD compared to THC, it is bushier, shorter, grows up to 2 metres, and is adapted to cooler climates.

Effects:

Cannabis *indica* strains are known for having a much higher CBD content than *sativas*. One of the many functions of CBD is to moderate the effect THC has on the body and mind. Thus, *indica* strains have a very different effect than *sativas*. These effects include:

- A body buzz; acting as a muscle relaxant
- Reduces inflammation
- Effective pain relief/management
- Aids sleep
- Acting as a sedative
- Increases food appetite
- Increases dopamine production
- Relieving stress and anxiety

ISSN No. 2321-2705 | DOI: 10.51244/IJRSI |Volume XII Issue II February 2025

III. Cannabis *Sativa*: Cannabis *sativa* are physically the largest of the three families, and are also probably the most popular. They originated in the wilds of equatorial countries, between 30 degrees north and 30 degrees south of the equator. In these equatorial countries, the hours of daylight do not fluctuate throughout the year in the same way it does across the rest of the globe thus, the plants have evolved to take advantage of this, and continue to grow as they flower. For this reason, *sativa* plants tend to look a lot more airy and loose and have a longer average flowering time than the *indica* or *ruderalis* variety, with a proportionally higher yield than their other family counterparts (**World Health Organisation – W.H.O, 1997)**.

The leaf of cannabis *sativa* plants are long and spindly, grows around 4.5 metres with laxly spaced branches and is often described as being finger-like; much like the stereotypical representation of a cannabis leaf. More so, the flowers of the female plant are arranged in racemes and can produce hundreds of seeds while the male plants shed their pollen and die several weeks prior to seed ripening on the female plants (**World Health Organisation – W.H.O, 1997**).

Effects:

The very high concentrations of THC and relatively low levels of CBD of Cannabis *sativa* plants, which have been further strengthened by human breeding tends to result in *sativas* having the following effects:

- A cerebral head buzz
- Energizes and uplifts
- Motivation
- Focusing and/or increasing alertness
- Inspiring and increasing creativity
- Reduces nausea
- Helps relieve depression/promotes a sense of wellbeing
- Stimulates appetite

Phytochemical Constituent of Cannabis *Sativa*

The table below shows the Qualitative phyto-chemical screening of Cannabis *sativa* crude leaf extract obtained from Jos, Plateau State, Nigeria.

Table 1 showing the Phyto-chemical Constituents of Cannabis *sativa*

Source: Audu *et al.*, (2014)

PHYTOCHEMICAL	QUALITY	COLOR	TEST
Alkaloid	+ + +		
Saponin	-		
Flavonoids	+ +		
Tannins	-	Orange	Dragendoff's
Cardiac Glycosides	+ + +	Light Yellow	Lead acetate
Balsam	-	Reddish Brown	Keller-Killani
Phenols	-	Reddish Brown	Burchard
Terpenes & Steroids	+ + +	Violet	
Resins	+ + +		
Volatile Oils	-		

- +++ High presence ++ moderate presence – Absence

ISSN No. 2321-2705 | DOI: 10.51244/IJRSI |Volume XII Issue II February 2025

Uses of Cannabis

The ingestion of cannabis has a variety of health effects with some being beneficial and some, not so beneficial. Cannabis combines many of the properties of alcohol, tranquilizers, opiates and hallucinogens and it's response varies according to the dose, route of administration and form in which it is consumed. It's most widely and popular means of usage is in its dry herbal form but more users ingest it in salads, tea additives, ingredient in drugs and vegetable juices **(Graham, 1998).**

Despite its diminutive size, hemp is increasingly spoken of as one of the most nutritionally complete food sources in the world, second only to soybean in protein content of 25%:32% ratio **(Hall & Solowji, 1998)**. The reason for its being so valued as listed by **Merzouki *et al.*, 2000 & Nath *et al.*, 1997** include;

1. It is used in convulsions, otalgia, abdominal disorders, malarial fever, dysentery, diarrhoea, skin diseases, hysteria, insomnia, gonorrhoea, colic, tetanus and hydrophobia.

2. The bark is tonic and useful in inflammations, haemorrhoids and hydrocele while the seeds are carminative, astringent, aphrodisiac, antiemetic and anti-inflammatory.

3. The resin is usually smoked to allay hiccup and bronchitis in addition to being used to treat insomnia, headaches, neuralgia, migraine, mania, whooping cough, asthma, dysuria.

4. The inflorescence of female cannabis plant is intoxicating, stomachic, soporific, abortifacient and useful in convulsions.

5. It is useful in relieving pain in dysmenorrhoea and menorrhoea.

6. In the brain and Central Nervous System, it produces alteration in motor behaviour, perception, cognition, memory, learning and regulation of body temperature **(Huestis *et al.*, 1992a).**

However, the use of ethanolic extract of cannabis has been reported by **Sailnani & Moeini, 2007** to reduce sperm count whereas, chronic consumption of its leaves has been reported by **Varsha *et al.*, 2013** to have detrimental effects on almost every body system. In respiratory system, the smoke is potentially carcinogenic, reduces lung function and increases chances of bronchitis, pharyngitis and asthma-like conditions **(Huestis *et al.*, 1992b).** Cannabis is also reported to antagonise the effect of both endogenous and exogenous insulin in addition to having immunosuppressant and endocrine effects **(Mckim, 2002).**

Pharmacokinetics and Pharmacodynamics of Cannabiniods

1. Pharmacokinetics

The kinetics of cannabinoids is much the same for males and females and the same for frequent and infrequent users **(Grotenhermen, 2003)**. However, Pharmacokinetics is an important field for the understanding of drug actions because the time course of the absorption, distribution, metabolism and excretion of drugs allows us to study how differences in kinetic properties may influence the use, misuse and abuse of psychoactive drugs **(Busto *et al.*, 1989).**

The pharmacokinetic properties of a drug liable to increased abused/self-administration include; rapid absorption, rapid entry into specific brain regions, high oral bioavailability, low protein binding, short half-life, small volume of distribution and high free drug clearance. Whereas, Pharmacokinetic properties may also play an important role in predicting dependence and the abuse potential of drugs but the pharmacokinetic properties associated with drug dependence are long half-life and low free drug clearance. Therefore, the drug must be present in the body at high enough concentrations and for sufficient time to permit tolerance (tachyphylaxis) to develop **(Busto *et al.*, 1989).**

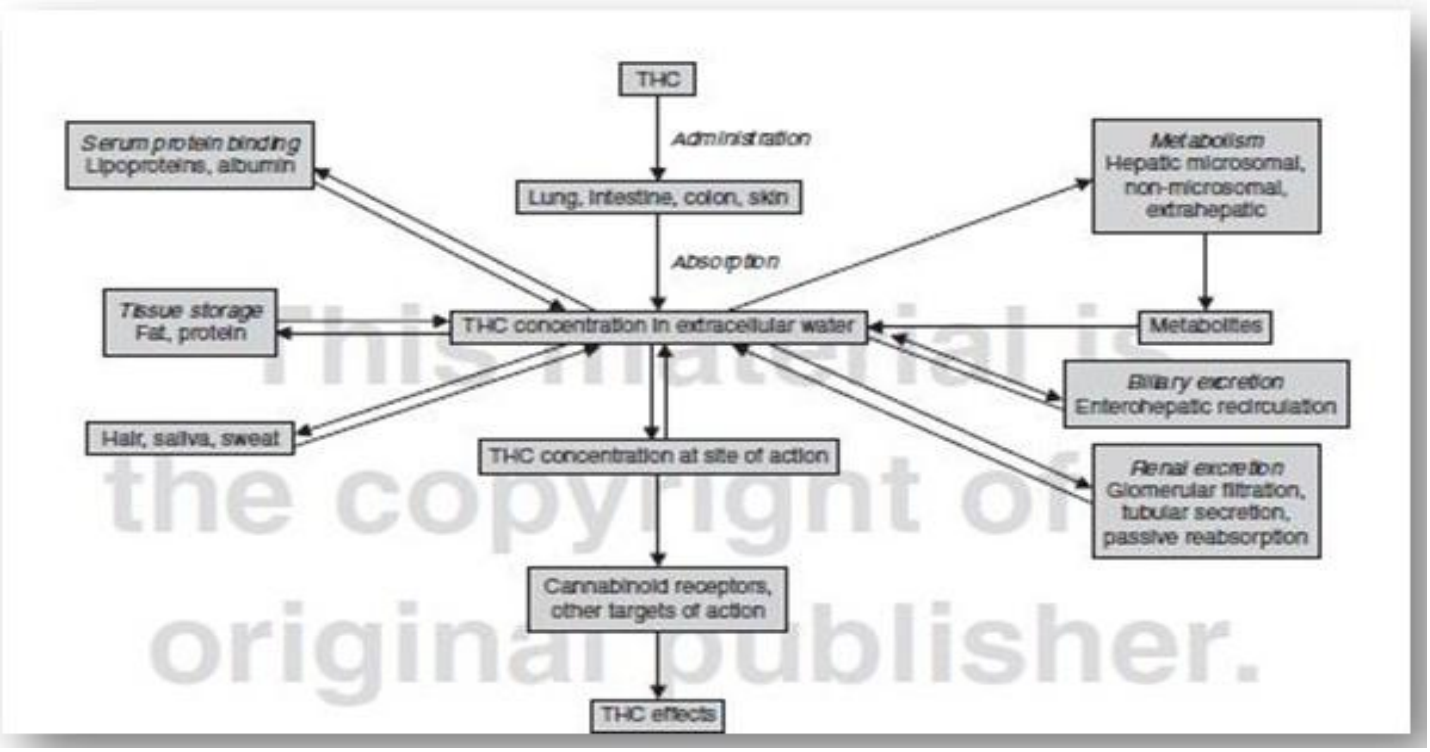
The products from Cannabis are commonly ingested orally via baked foods or liquids or in capsules (as dronabinol) and inhaled by smoking a cannabis cigarette. Other routes of administration and delivery forms

ISSN No. 2321-2705 | DOI: 10.51244/IJRSI |Volume XII Issue II February 2025

have been tested for therapeutic purposes. The rectal route with suppositories has been applied in some patients while dermal sublingual administrations are being investigated. Other methods include eye drops to decrease intraocular pressure in addition to aerosols and inhalation with vaporisers to avoid the harm associated with smoking **(Grotenhermen, 2003**).

Fig. 1 Diagram showing Pharmacokinetic properties of Δ9-tetrahydrocannabinol (THC)

Extracted from: **Grotenhermen, (2003)**



If cannabis is taken orally, the amount absorbed is about 25-30% of that obtained by smoking and the onset of effect(s) is between 5mins - 2hrs. Though, duration of action may be prolonged **(Maykut, 1985).** Upon entering the bloodstream, cannabinoids are distributed rapidly throughout the body, reaching first the tissues with the highest blood flow (brain, lungs, liver, etc.). Within the brain, cannabinoids are differently distributed, reaching high concentrations in neocortical areas (especially the frontal cortex), limbic areas (hippocampus and amygdale), sensory areas (visual and auditory), motor areas (basal ganglia and cerebellum) and the Pons **(McIsaac *et al.*, 1971).**

Approximately 50% of the THC and other cannabiniods present in a cannabis cigarette enter the mainstream smoke and are inhaled. The amount absorbed through the lungs depends on smoking style. In experienced smokers who inhaled deeply and hold the smoke in the lungs for some seconds before exhaling, virtually all of the cannabiniods present in the mainstream smoke enter the bloodstream **(Busto *et al.*, 1989; Maykut, 1985)**. Subjective and objective effects are perceptible within seconds and fully apparent within minutes from the start of smoking. 2.5mg of THC in a cigarette is enough to produce measurable psychological physical effect in occasional cannabis users **(Gold, 1991; Maykut, 1985)**.

Being highly fat soluble, cannabiniods accumulate in fatty tissues from which they are very slowly released back into other body compartments, including the brain. The plasma elimination half-life of THC is approximately 56hrs in occasional users and 28hrs in chronic users **(Busto *et al.*, 1989).** However, because of sequestration in fat, the tissue half-life is approximately 7 days and complete elimination of a single dose may take up to 30 days **(Maykut, 1985).**

With repeated dosage, high concentrations of cannabinoids can accumulate in the body and continue to reach the brain. Cannabinoids are metabolized in the liver, forming more than 20 metabolites, some of which are psychoactive and many of which have plasma elimination half-lives of order of 50hrs. Further metabolism

ISSN No. 2321-2705 | DOI: 10.51244/IJRSI |Volume XII Issue II February 2025

produces inactive metabolites of which 15-30% are excreted in urine. Active and inactive metabolites are also excreted into the intestine and bile and approximately 15% are reabsorbed, prolonging the action of cannabis, while about 35-65% are finally eliminated in the faeces **(Maykut, 1985).**

Table 2: Chart showing the Mean cumulative cannabinoid excretion in Humans

SOURCE: **Grotenhermen (2003)**

Subjects/route	Urine (%)		Faeces (%)		Total (%) at 72h	% of total in urine
						at 72h
	24h	72h	24h	72h		
Women/Intravenous	11 ± 2	16 ± 3	9 ± 11	26 ± 19	42	38.1
Men/intra-venous	10 ± 5	15 ± 4	14 ± 11	35 ± 11	50	30.0
Women/oral	12.5 ± 3.0	15.9 ± 3.6	9 ± 11	48 ± 6	63.9	24.9
Men/oral	10.3 ± 2.1	13.4 ± 2.0	24 ± 42	53 ± 18	66.4	20.2

2. Pharmacodynamics

The majority of phytocannabinoid effects are mediated through agonistic or antagonistic actions at specific receptors sites. Cannabinoid receptors and their endogenous ligands together constitute the 'endogenous cannabinoid system' or the 'endo-cannabinoid system' that is teleologically millions of years **(Grotenhermen, 2003).** CB receptors are present in the brain particularly in regions involved in cognition, memory, reward, anxiety, pain, sensory perception, motor co-ordination and endocrine function **(Adams and Martin, 1996**; **Herkenham, 1995; Matsuda *et al.*, 1990; Musty *et al.*, 1995)**. CB_2 receptors are also found in the spleen and other peripheral tissues and may play a role in the immuno-suppressive actions of cannabinoids **(Musty *et al.*, 1995).** The physiological ligands for these receptors appear to be a family of anandamides which are derivates of arachidonic acid, related to prostaglandins **(Devan *et al.*, 1992; Pertwee, 1995)**. It appears that there is an endogenous system of cannabinoid receptor and anandamides which normally modulate neuronal activity by effects on cyclic AMP formation and Ca^{2+} and K^{+} ion transport **(Matsuda et al, 1990; Perwee, 1995; Musty *et al.*, 1995)**.

However, the physiological function of this system is not understood but it is thought to have important interaction with opioid, GABAergic, dopaminergic, nor-adrenergic, serotonergic, cholinergic, glucocorticoid and prosterglandin systems **(Gardner, 1992; Martin, 1995; Adams and Martin, 1996).** The many effects of exogenous cannabinoids derived from cannabis almost certainly result from perturbation of the complex system, but the exact mechanisms are not clear.

Systemic Effects of Cannabis in the Body

1. Effect on Respiratory System

The smoke from herbal cannabis preparation contains all the same constituents (apart from nicotine) as tobacco smoke, including carbon-monoxide, bronchial irritants, tumour irritators (mutagens), tumour promoters and carcinogens **(British Medical Association, 1997**). The tar from a cannabis cigarette contains higher concentration of benzanthracenes and benzpyrenes, both of which are carcinogens than tobacco smoke. It has been estimated that smoking a cannabis cigarette results in approximately, a five-fold greater increase in carboxyl-haemoglobin concentration, a three-fold greater amount of tar inhaled and retained in the respiratory tract and one-third more tar than smoking a tobacco cigarette. This is mainly due to the way a cannabis joint is

ISSN No. 2321-2705 | DOI: 10.51244/IJRSI |Volume XII Issue II February 2025

smoked without filter, with deep and prolonged inhalation in addition to having a higher combustion temperature than tobacco **(Benson and Bently, 1995).**

Chronic cannabis smoking is associated with bronchitis and emphysema. It has been calculated that smoking 3-4 cannabis cigarettes a day is associated with the same evidence of acute and chronic bronchitis and the same degree of damage to the bronchial mucosa as 20 or more tobacco cigarette a day **(Benson and Bently, 1995)**. Prospective studies of the long term effects on the lungs of chronic cannabis users are lacking but some authors suggests that chronic airways disease and bronchogenic carcinoma may be as great a risk as with tobacco smoking. More so, there appears to be an increased incidence of rare forms of oro-pharyngeal cancer in young people who smoke cannabis chronically **(Ashton, 2011).**

The Institute of Medicine, in its 1999 report for the U.S. White house Office of National Drug Control Policy, conducted a review of the scientific evidence to assess the potential health benefits and risks of cannabis and its constituent cannabinoids. On the issue of cannabis smoke, the report entitled Marijuana and Medicine: Assessing the Science Base, concluded that chronic cannabis smoking might lead to acute and chronic bronchitis and extensive microscopic abnormalities in the cells lining the bronchial passageways some of which may be premalignant **(Barsky *et al.*, 1998).**

2. Effects on Digestive System

One of the basic effects of Cannabis *sativa* on the digestive system is that it increases the rate of digestion in the stomach and small intestinal wall by increasing the rate of gastric acid production which in some cases increases the rate of peptic ulcer infections in the gastrointestinal tract **(Schuber, 2008).**

The consumption of cannabis affects the digestive system both directly and indirectly because smoking it makes one tired and less likely to eat and making this a routine causes the body, stomach, and the entire gastrointestinal tract to slower digestive pattern and less weight gain. More so, when cannabis sativa is smoked, the body's metabolism is accelerated which when the digestive system works faster, food is digested at a faster rate than normal **(Wikispace, 2013).**

3. Effect on Cardiovascular System

In some of the earliest report of the cardiovascular effects of cannabis exposure, even a single administration to healthy cannabis users led to an increase in both pulse rate and blood pressure resulting in an increase in myocardial oxygen demand. Most cases of cannabis-associated acute coronary syndrome occur within 1 hour of exposure and are generally associated with coronary arteries that appear angio-graphically normal yet are prone to develop spasm, coronary thrombus, or coronary microcirculatory dysfunction. Acute coronary syndrome may also occur years after frequent use with no apparent precipitating factors other than cannabis use **(Thomas *et al.*, 2014).**

Acute coronary syndrome triggered by cannabis exposure may include angina pectoris, myocardial infarction, and sudden cardiac death. In a 2001 publication by **Mittleman *et al.*, (2001),** three thousand eight hundred and eighty two (3,882) patients with acute myocardial infarction were assessed for cannabis use, revealing a 4.8-fold increase in the risk of myocardial infarction in the first hour after cannabis use compared to non-users.

The coronary effects of cannabis exposure can also result in cardiac arrhythmias and/or sudden cardiac death. **Kochar and Hosko (1973)** investigated the effects of THC on persons with normal electrocardiograms at baseline where most volunteers had characteristic ST-segment elevation with decrease in Amplitude of T-waves in addition to having occasional premature ventricular contractions. Sudden cardiac death has been reported in cannabis users but it appears to be a relatively rare event and less frequent than reports associated with the use of other illicit drugs **(Tormey, 2012; Hser *et al.*, 2012)**.

4. Effect on Endocrine and Reproductive Systems

Ethanolic extract of cannabis sativa administered intraperitonially to male rats has been reported to significantly decrease epididymal sperm count **(Sailani and Moeini, 2007)**. **Nwangwa et al., (2009)** studied the effect of

ISSN No. 2321-2705 | DOI: 10.51244/IJRSI |Volume XII Issue II February 2025

cannabis *sativa* (20mg in 5% ethanol) on testosterone level and seminal fluid analysis of male wistar rats weighing between 120-150g and found a statistically significant decrease in percentage motile sperm and an increase in the percentage dead sperm. The increase in the sperm count was not statistically significant and the changes in testosterone hormonal levels from their result were also not statistically significant.

Further reports by **Kolodny *et al.*, (1974)** showed that frequent cannabis users had lower testosterone levels than occasional cannabis users due to temporal reductions observed immediately after intake. In another study, heavy chronic users were found to have similar testosterone levels compared to casual users at baseline and did not experience any significant alterations in testosterone after a 21-day period of intense cannabis smoking within a controlled research setting **(Mendelson *et al.*, 1974).**

More so, a 58% decrease in sperm concentration was reported in chronic users after intensive marijuana smoking without a significant change in LH or testosterone while a reduction in testicular size were observed in rodents and dogs following the administration of cannabis extract **(Hembree *et al.*, 1976; Dixit *et al.*, 1977).** Women who smoke cannabis may have a slightly increased risk of infertility due to an ovulatory abnormality, which was shown in a case control study of female recreation drugs users with primary infertility **(Mueller *et al.*, 1990)**.

Similarly, the administration of cannabis to rats blocked the LH surge normally leading to ovulation and abolished the ovulatory cycle in rats and rabbits **(Dixit *et al.*, 1975; Asch *et al.*, 1979)**. Reports by **Mendelson *et al.*, (1986)** also showed a 30% decrease in LH in women compared to control one(1) hour after administration of a marijuana cigarette (1g or 1.8% THC) during the luteal phase but reported no effects in the follicular phase. In another study, a marijuana cigarette given in periovulatory stage increased LH levels while no acute change in LH was seen in menopausal women **(Mendelson & Mello, 1984; Mendelson *et al.*, 1985)**.

Animal studies have demonstrated an acute reduction of prolactin levels after THC administration in both rodents and primates. It was also observed that prolactin was reduced by a maximum of 84% in ovariectomized female monkeys and in 74% males at about 30-90 minutes of a single THC injection **(Bromely and Zimmerman, 1976; Smith *et al.*, 1976)**. However, Cannabinoids have been shown to inhibit the secretion of Growth Hormone (GH) due to stimulation of somatostatin release. Another reason is because 4 days of oral THC blunted the normal GH response to insulin-induced hypoglycaemia which is the "gold standard" test of GH axis integrity **(Rettori *et al.*, 1988).**

5. Effect on Pregnancy

In women, cannabis consumption was reported to lower levels of follicle-stimulating hormone (FSH) and luteinizing hormone (LH), and may affect the menstrual cycle. Although, these effects were evidently reversible and disappeared once the drug was discontinued **(Hollister, 1986; Maykut, 1985).**

Evaluation for differences in birth weight, birth length, head circumference, chest circumference, gestational age, neurological development, and physical abnormalities in newborn babies of women who used cannabis before and during pregnancy with the babies of women who weren't exposed to cannabis have found no differences between these babies **(Witter and Niebyl, 1990).** However, in a study of 12,000 women in which 11% used marijuana, it was observed that there were shorter gestation periods, longer time of deliveries, lower birth weights and higher rates of deformities **(Hollister, 1986).**

6. Effect on the Immune System

Given the long history of large-scale cannabis use by young adults in western societies, the absence of any epidemics of infectious disease makes it unlikely that cannabis smoking produces major impairments in the immune system. However, what is more difficult to exclude is the possibility that chronic heavy cannabis use produces minor impairments in immunity due to it's ability to weaken the immune system and interrupt the maturation of white blood cells. This is because Cannabis sativa reduces total White Blood Cells significantly as a result of significant reduction of neutrophils and lymphocytes percentages which in effect would produce small increases in the incidence of common bacterial and viral illnesses among chronic cannabis users **(Coates *et al.*, 1990; Amna *et al.*, 2011).**

ISSN No. 2321-2705 | DOI: 10.51244/IJRSI |Volume XII Issue II February 2025

An epidemiological study by **Polen *et al.*, (1993),** which compared health service utilization by "non-smokers" and "daily cannabis-only smokers," suggested a small increase among cannabis smokers in the rate of presentation of respiratory conditions. This finding remains suggestive, however, because infectious and non-infectious respiratory conditions were considered together. The finding that cannabinoids produce minor impairments in immunity would therefore cast doubt on the therapeutic value of cannabinoids in immunologically compromised patients, such as those undergoing cancer chemotherapy or those with AIDS.

A prospective study of human immunodeficiency virus (HIV)-positive homosexual men have found that cannabis use was not associated with an increased risk of progression to AIDS but these patients who use cannabis do face an increase risk of contracting the pulmonary disease aspergillosis. This disease, caused by fungal spores that sometimes contaminate improperly stored cannabis has only been reported in smokers with immune-suppression disorders. Thus, careful screening of cannabis supplies for aspergillus spores and other contaminants would make cannabis safer for AIDS patients **(Chusid *et al.*, 1975).**

7. Effect on Blood and Haemostasis

Cannabis has been reported to increase haemoglobin (HB) concentrations, Packed cell volume (PCV), platelet and White Blood Cell (WBC) counts while a shortened bleeding and clotting times, prothrombin and partial thromboplastin times and improve wound healing were observed in a study conducted on male albino wistar rats **(Oguwike *et al.*, 2016).**

Haematological studies in rats (weighing between 70-200g) and men (18-60 years old) by **Mukhtar and Elbagir, (2011)** showed alterations in haematological indices. Their study showed that petroleum ether extract of Cannabis *sativa* (0.2mg/g and 0.6mg/g) significantly decreased red blood cells (RBC) count and total WBC count in rats but these parameters were not changed in addicted men. Also their study showed that Neutrophils and lymphocytes percentages decreased and eosinophils increased significantly in all treated groups of rats compared to the control group. In the addicted men, eosinophils and monocytes showed significantly lower levels compared to the control group, but lymphocytes percentages were elevated in all addicted men compared to the control group. But Hb concentration was not significantly different in all groups of rats and men.

Another study by **Obembe *et al.*, (2015),** on haematological and immunological effects of Cannabis *sativa* in rats showed that cannabis (0.8 mg/100 g body weight) significantly increased RBC Count, HB concentration and platelet count and decreased total WBC count but had no significant effect on PCV. Their result also showed significant decrease in lymphocytes, monocytes and neutrophils counts but Eosinophils and basophils counts were significantly increased following cannabis intake.

Eledo *et al.*, (2015) investigated the effects of cannabis on haematological parameters of some men in yenagoa, Nigeria and found no significant differences in PCV, Hb concentration, Total WBC, RBC, platelet, monocyte and basophils counts as well as prothrombin time (PT) and partial thromboplastin time between the test subjects and controls. There was a significant increase in erythrocyte sedimentation rat (ESR), lymphocyte count and eosinophils count in the test subjects when compared with the Controls observed from their study.

In a completely randomized design study on Effects of Marijuana Smoking on some Haematological Parameter of Smokers by **Oseni *et al.*, (2006),** it was reported that haematological parameters were not significantly different between the test and control subjects. Though, within normal range, the values observed for total leucocytes, neutrophils, lymphocyte, monocyte and platelet counts were marginally lower in the test subjects, while values observed for PVC, Hb concentration and eosinophils count were marginally higher. Occurrence of low lymphocyte count was specifically observed in 12.5% of test subjects while occurrence of high eosinophil count was specifically observed in 4.2% of test subjects.

8. Effect on Visual System

A study by **Dasilva *et al.*, (2012)** quantified the functional action Cannabis on cannabinoid-1 (CB-I) receptors within the Lateral Geniculate Nucleus (LGN) and found two populations; 28% were excited by an antagonist

ISSN No. 2321-2705 | DOI: 10.51244/IJRSI |Volume XII Issue II February 2025

and 72% were inhibited. When activated artificially (as would be with cannabis) the visual signals were altered while with excitation activity, there was a decrease in the signal-to-noise ratio and an increase in variability. With altered inhibition; which accounts for over 70% of the cells in the LGN, there was an increase in the signal-to-noise ratio with reductions in variability. They concluded that the abnormal signals originating from the Lateral Geniculate Nucleus (LGN) with artificial stimulation of the cannabinoid receptors using cannabis and then travelling to the cortex would account for behavioural effects of cannabis.

Reductions in acuity have been reported secondary to cannabis consumption **(Dawson *et al.*, 1977).** However, reports by **Adam *et al.*, (1975)** did not find reductions in static acuity but did find reductions in dynamic acuity after cannabis consumption. The structural findings related to the cones in the retina koniocellular layers of the LGN offer an explanation for the functional findings of colour impairment with cannabis consumption. Several researchers have identified colour deficits along the blue axis. **Adam *et al.*, (1976)** further coined that dose-related impairment with the consumption of cannabis was identified using Farnsworth-Munsell 100 hue test and the findings were along the blue axis. The deficits were similar to those blue deficits that occur with retinal based pathology leading researchers to conclude that the origin of the dysfunction was in the retina itself. Dawson and colleagues supported the findings of significantly reduced colour vision function with decreased colour matches among those having consumed cannabis **(Dawson *et al.*, 1977).**

In a study reported in 2012 with the cooperation of law enforcement, 25 cannabis-using participants identified by urinalysis to have cannabis as the only intoxicant, found lack of evidence for deficits in eye movements **(Citak *et al.*, 2012)**. In the study of 20 adults using cannabis and cannabis combined with alcohol, researchers found that with cannabis alone the users showed impairment with the field sobriety test of one leg stand, but dysfunction in regards to Horizontal Gaze Nystagmus (HGN) were when cannabis was combined with alcohol **(Bosker *et al.*, 2012).** This study was conducted in Holland and used a product that contained 11% THC. This was considered to be the average potency of recreational and medicinal marijuana/cannabis in Holland. Recent studies comparing plant cannabis and the use of synthetic cannabis demonstrate a high rate of HGN among those using synthetic cannabis compared to those using plant cannabis. The rate of HGN was 50% in the synthetic group with 12% in the plant group **(Chase *et al.*, 2016).**

10. Effects of Cannabis on the Nervous System

The effect of cannabis on the Nervous system can be classified into three categories which include;

1. Psychiatric effect
2. Cognitive effect
3. Psychopharmacological effect

I. Psychiatric Effect: In healthy volunteers, relative to placebo, the administration of THC was associated with anxiety, dysphoria and positive psychotic symptoms **(Johnson *et al.*, 2012).** Anxiety and panic reactions are common reasons for the discontinuation of cannabis use **(Johns, 2001).** In high doses, Cannabis can produce a toxic phychosis in people without a history of mental illness and it's use can lead to many short term symptoms like depersonalisation, derealisation, dream-like euphoria, disorientation, delusions, hallucinations, paranoid ideas, impaired memory, reduced attention spans, disordered thinking with a labile effect, psychomotor agitation, irrational panic and emotional liability **(Johns, 2001).** However, these symptoms may be resolved within a week, followed by full recovery **(Crippa *et al.*, 2012)**.

II. Cognitive Effect: Despite the large number of related studies, there are conflicting opinions regarding the association between Cannabis use and cognitive disorder **(Iversen, 2005).** Cognitive deficits seem to be linked with the early onset of Cannabis use. There are associations between chronic cannabis use and dysfunction across a range of functions including aspects of memory, attention, executive functions, performance of complex mental processes, judgment, motor skills and reaction time **(Solowij and Pesa, 2010; Tait *et al.*, 2011; Crean *et al.*, 2011; Fisk and Montgomery, 2008)**.

A recent study showed cognitive deficits in young Cannabis users (18-29 years old) even in the absence of axis-1 disorders and a history of other illicit drug use **(Grant, 2012).** These neuro-cognitive deficits persisted for a few days following the cessation of Cannabis intake **(Pope *et al.*, 2001).** Although, other investigators have

ISSN No. 2321-2705 | DOI: 10.51244/IJRSI |Volume XII Issue II February 2025

suggested that these deficits may persist for a month or longer **(Solowij, 1995)**. However, cessation of Cannabis use did not fully restore neuropsychological functioning among adolescent-onset cannabis users **(Meier *et al.*, 2012).**

More so, the use of Cannabis is linked to neurological deficits including the impairment of motor co-ordination and reaction time as it increases the risk of road accidents in drivers who are under its influence. This is because Cannabis remains the second most cited drug after alcohol in car crashes **(Hall *et al.*, 2001)**.

Perhaps, the most robust evidence linking Cannabis use and driving comes from a meta-analysis of nine (9) studies conducted by Researchers at Columbia University's College of Physicians and Surgeons where more than a quarter of all seriously injured drivers admitted to a Level-1 shock trauma centre, tested positive for Cannabis **(Romano and Voas, 2011).** After reviewing these epidemiologic studies from the past twenty years, they found that Cannabis use was linked to heightened risk of crash involvement even when controlling from multiple different variables. They further discovered that the risk of crash involvement increased along with an increase in Cannabis potency (tested through urinalysis) and self-reported frequency of use.

Another research conducted at the University of Auckland, New Zealand also shows that Cannabis use and auto crashes are strongly associated. The research found that habitual cannabis users were 9.5 times more likely to be involved in crashes, with 5.6% of people who had crashed having taken the drug when compared to 0.5% of the control group **(Blows, 2005).**

III. Psycho-Pharmacological Effect: Acute cannabis use is associated with subjective symptoms of euphoria, continuous laughter and talkativeness, sedation, lethargy, intensification of ordinary sensory experiences, perceptual distortion, and social withdrawal **(Johnson, 1990).** Physical signs of conjunctival hyperaemia, increased appetite and food consumption, dry mouth, increased blood pressure and tachycardia as well as acute bronchodilator effects have also been reported. Increased Heart rates by 20-50% within a few minutes to a quarter of an hour with a lasting effect of up to 3 hours have also been reported **(Hall and Solowij, 1998).**

General Adverse Effect of Cannabis *Sativa*

Some potential adverse effects of Cannabis *sativa* when taken in high doses or over a long period as reported by **Greydanus *et al.*, (2012)** include;

Addiction (physiologic), Withdrawal syndrome, Dependence (psychological) with heavy use-tolerance, Variety of negative psychological reactions which include: anxiety, hallucinations, violent behaviour, depression and fear, Overt precipitation of psychosis or depression, Insomnia (can be chronic and improved with trazadone), Memory spans that are impaired, blunted reflexes, flu-like reaction (after stopping the drug between 24-60hrs, lasting up to 2weeks), confusion and cognition impairment, alteration of time perception and motivational syndrome (lose of interest in school or work success). However, Physiologic responses can include cough, bronchospasm, bronchitis, amenorrhea and immunologic dysfunction.

Cannabis abuse may produce adverse effects on the cardiovascular system since its chemical constituent causes an increase in heart rate based on a dose-dependent ratio. It can cause an increase in the risk of myocardial infarction (4-8 folds) within the hour after use and also provoke angina in patients with heart disease **(Hall and Degenhardt, 2009).**

However, some of the general effects of cannabis on the body are summarised as thus;

- **Cannabis Withdrawal Syndrome**

This syndrome occurs in frequent users who quit without seeking treatment **(Budney and Hughes, 2006).** The diagnostic criteria for withdrawal are irritability, anger or aggression, nervousness or anxiety; sleep difficulty (insomnia), weight loss due to decreased appetite, restlessness, depressed mood and physical symptoms causing significant discomfort like stomach pain, shakiness/tremors, sweating, fever, chills and headache **(Smith, 2002).**

ISSN No. 2321-2705 | DOI: 10.51244/IJRSI |Volume XII Issue II February 2025

- **Motivational Syndrome**

According to **Tennant and Groesbeck (1972),** heavy chronic cannabis users may experience a motivational syndrome described as a reduced capacity and motivation for the usual activities required for everyday life, loss of energy and drive to work and personality deterioration. The validity of this diagnosis remains uncertain **(Hall and Solowji, 1998).**

- **Cannabis-induced Depersonalisation**

Cannabis use has led to depersonalisation which is a disorder or an alteration in the subjective experience of reality. It is characterised by persistent or recurrent experiences of feeling detached (as though one is an outside observer of one's mental processes or body), alterations in body image (feeling like an automaton), time disturbances (feeling as if one's body or environment is dream-like) and visual distortions **(Spiegel *et al.*, 2011; Szymanski, 1981)**. The depersonalisation experience causes clinically significant distress or impairment in social, occupational or other important areas of functioning.

Therapeutic Function of Cannabis

Pain Management: According to **Pertwee 1995**, Cannabis has analgesic, muscle relaxant and anti-inflammatory actions. In addition, it exerts anxiolytic, hypnotic and antidepressant effects **(Fabre and McLendon, 1981; Carlin and Cunha, 1981)** and may have anticonvulsant actions as reported by **Grotenhermen and Russo, 2002**.

The analgesic effect of cannabis appears to be exerted by non-opioid mechanisms as unlike the "rewarding" effects (release of dopamine from the nucleus accumbens). Cannabinoid-induced analgesia is not reversed by naloxone which suggests that cannabinoids would be ideal candidate for use in chronic pain management, either on their own or in combination with other drugs, including opioids, antidepressants, muscle relaxants and anticonvulsants **(Grotenhermen and Russo, 2002; Hamann and Divadi, 1999).**

A few controlled studies involving a total of only 20 patients showed that oral THC (2.5-15mg/day) relieved spasticity and tremor which improved the general well-being in some patients with multiple sclerosis **(Petro and Ellenberger, 1981; Underleider *et al.*, 1988)**. Another report by **Noyes *et al.*, 1975** also proves that THC provided significant relief compared with placebo in patients with cancer pain and 20mg of oral THC was equivalent in analgesic potency to 120mg of codeine. However, sedation and mental clouding were common side effects.

Treatment of Gastrointestinal Disorder: Cannabidiol (CBD) which is the second most abundant cannabinoid on Cannabis plant has been shown to reduce hyper-motility, inflammation and tissue damage in experimental models of G.I diseases **(Capasso *et al.*, 2001; Borrelli *et al.*, 2009).**

The abundant cannabinoid receptors in the gut represent an excellent target to treat G.I disorders as the receptors are shown to be up-regulated in the intestinal tissue of patients suffering from Inflammatory Bowel Disease (IBD) **(Wright *et al.*, 2008).** The activation of these hyper-expressed cannabinoid receptors can have protective and therapeutic effect against disorders of the G.I tract **(Capasso *et al.*, 2008).** Cannabinoids alter how the gut feels, affects the to and fro signals the brain sends to the gut and modulate the actions of the G.I tract itself **(Grotenherman, 2004; Izzo *et al.*, 2001).**

Many researchers have concluded that pharmacological modulation of the endogenous cannabinoid system provides new treatment options for a number of gastrointestinal diseases including nausea and vomiting, gastric ulcers, irritable bowel syndrome, Crohn's disease, secretory diarrhoea, paralytic ileus and gastro-oesophageal reflux disease **(DiCarlo and Izzo, 2003; Hunt and Tougas, 2002; Izzo *et al.*, 2000)**. The experience of patients with these GI disorders shows that for broad-spectrum relief, cannabis is highly effective and frequently helps when other treatment options prove ineffective **(Hazekamp *et al.*, 2006).**

Haematological Indices

The consumption of Cannabis seems to have systemic effects, so; all organs, tissues, cells and blood which is

ISSN No. 2321-2705 | DOI: 10.51244/IJRSI |Volume XII Issue II February 2025

the connective tissue to all these systems may be affected. More so, the analysis of haematological indices through the use of appropriate laboratory techniques in blood cell examination and the determination of different parameters could provide vital information on how these systemic effects following cannabis consumption are established.

1. Blood:

Blood is classified as a connective tissue consisting of cells and cell fragments surrounded by a liquid matrix **(Rod *et al.*, 1992).** It is regarded as a modified connective tissue because some of the cells in it have close affinities to the general connective-tissue cells in addition to having cellular elements that are separated by a considerable amount of "intercellular substance" **(Indebir, 2006).**

The cells and cell fragments in blood are called formed elements while the fluid matrix is the plasma. However, blood makes up about 8% of the total body weight of humans and the blood volume of an average adult is about 4-5ltrs in females and about 5-6ltrs in males **(Rod *et al.*, 1992).**

The blood cells present in blood are mainly red blood cells, white blood cell and platelets. The most abundant cells in vertebrate's blood are red blood cells which contain haemoglobin and facilitates the transportation of oxygen by reversibly binding to this respiratory gas in addition to greatly increasing its solubility in blood. In contrast, carbon dioxide is almost entirely transported extra-cellularly and dissolved in plasma as bicarbonate ion. By volume, the RBC constitutes about 45% of whole blood, the plasma about 54.3% and WBC about 0.7% **(Barrett *et al.*, 2012).**

2. Functions of Blood

Blood performs many important functions within the body including. These functions as listed by **Barrett *et al.*, (2012)** are;

- Supply of oxygen to tissues
- Supply of nutrient such as glucose, amino acids and fatty acts.
- Removal of waste such as carbon dioxide, urea and lactic acid.
- Immunological functions including circulation of white blood cells and detection of foreign materials by antibodies.
- Coagulation: the act of blood clotting that occurs to stop the bleeding after one gets a cut.
- Messenger functions, including the transport of hormones and the signalling of tissue damage.
- Regulation of body P^H and core body temperature
- Hydraulic function

3. Production of Blood Cells

The process of blood cell formation, called hematopoiesis or hemopoiesis, begins in the yolk sac, which lies outside the embryo. Later in development, blood cells are manufactured in the liver and spleen, and afterwards formed in bone marrow **(Shier *et al.*, 2007**).

At first, lymphocytes are formed along other cells of blood in the bone marrow, but later they are formed mainly in lymphoid tissue **(Inderbir, 2006).** In postnatal life, blood formation is confined to bone marrow and lymphoid tissues. However, under condition in which the bone marrow is unable to meet normal requirements, blood cells formation may start in the liver and spleen; a process referred to as extra-medullary haemopoiesis **(Inderbir, 2006).**

There have been considerable controversies regarding the origin of various types of blood cells. The monophyletic theory holds that all types of blood cells are derived from a common stem cell; while the polyphyletic theory has it that, there are several independent types of stem cells. There is no doubt that all blood

ISSN No. 2321-2705 | DOI: 10.51244/IJRSI |Volume XII Issue II February 2025

forming cells in the embryo are derived from the mesenchyme and that the earliest stem cells (haemocytoblasts) are capable of forming all types of blood cells. These stem cells give rise to the immediate progenitors of the various types of blood cells; **proerythroblast** from which erythrocytes develop; **myoblasts** from which granulocytes develop; **lymphoblasts** from which lymphocytes develop; **monoblast** from which monocytes develop and **megakaryoblasts** from which platelets develop **(Indebir, 2006).**

4. Components of Blood Cells and their Distinctive Functions

There are three types of blood cells. These are identified by **Shier *et al.*, (2007)** to include;

1. Red Blood Cells (Erythrocytes)
2. White Blood Cells (Leucocytes)
3. Platelets (Thrombocytes)

I. Red Blood Cells – RBC (Erythrocytes): According to Holes 1993, Red Blood Cells are tiny, approximately 7.5µm in diameter and comprises more than 99% of blood cells. The average number of red blood cells per cubic millimeter of blood in normal men is 5,200,000 (±300,000), in normal women it's 4,700,000 (±300,000) while persons living at high altitudes have greater numbers of them **(Hall, 2011).** The main component of erythrocyte is the pigmented protein, hemoglobin which occupies approximately one third of the total cell volume and accounts for its red colour **(Rod *et al.*, 1992).**

Under normal conditions, about 2.5 million erythrocytes are destroyed every second. This amount seems like a staggering loss of erythrocytes until it is realized that the loss represents only about 0.00001% of the total 25 trillion erythrocytes contained in the normal adult circulation. However, erythrocytes normally stay within the circulation for about 120 days in males and 110 days in females but the old, damaged or defective erythrocytes are removed from the blood by macrophages located in the spleen, liver and other lymphatic tissues while the 2.5 million lost erythrocytes are usually replaced by the production of an equal number of erythrocytes at every second **(Rod *et al.*, 1992).**

The Functions of RBCs as identified and explained by **Sembulingam and Sembulingam, 2012** include;

1. The role of transporting oxygen from the lungs to the tissues. This is because RBCs contain a substance called haemoglobin which combines with oxygen to form oxy-haemoglobin and about 97% of oxygen in blood is transported in this form.

2. RBCs also transport carbon dioxide from the tissues to the lungs. Haemoglobin combines with carbon dioxide and form carb-haemoglobin and about 30% of carbon dioxide is transported in this form.

3. RBCs perform the buffering action in blood. Haemoglobin functions as a good buffer. By this action, it regulates the hydrogen ion (H^+) concentration thereby, playing a role in the maintenance of acid-base balance.

4. RBCs carry blood group antigens like antigen-A, antigen-B and Rhesus (Rh)-factor. This helps in the determination of blood group and helps to prevent reactions due to incompatible blood transfusion.

II. White Blood Cells - WBC (Leucocytes): The leukocytes, also called white blood cells, are the mobile units of the body's protective system. They are formed partially in the bone marrow (granulocytes and monocytes and a few lymphocytes) and partially in the lymph tissue (lymphocytes and plasma cells). After formation, they are transported in the blood to different parts of the body where they are needed **(Hall, 2011). Shier et al (2007),** further stated that Leukocytes are formed in response to hormones which are identified into two groups—interleukins and colony-stimulating factors (CSFs). He added that Interleukins are numbered, while most colony-stimulating factors are named for the cell population they stimulate.

The real value of the white blood cells is that most of them are specifically transported to areas of serious infection and inflammation, thereby providing a rapid and potent defense against infectious agents **(Guyton &**

ISSN No. 2321-2705 | DOI: 10.51244/IJRSI |Volume XII Issue II February 2025

Hall, 2006). Normally, there are five types of white blood cells in circulating blood. They differ in size, cytoplasm composition, shape of nucleus, and staining characteristics. Some of these cell types have granular cytoplasm and make up a group called granulocytes whereas, others lack cytoplasmic granules and are called agranulocytes **(Shier *et al.*, 2007).** These cells as listed by **Shier *et al.*, 2007** include:

1. Polymorphonuclear Neutrophils
2. Polymorphonuclear Eosinophils
3. Polymorphonuclear Basophils
4. Monocytes
5. Lymphocytes

The first three types of cells (the polymorphonuclear cells) all have a granular appearance hence are grouped into granulocytes while the other two fall under the agranulocyte due to the absence of granular appearance **(Shier *et al.*, 2007).**

Each of these WBCs type acts in a different way irrespective of their cytoplasmic property and their defensive functions in the body as listed by **Sembulingam and Sembulingam, 2012** include:

a. Neutrophils: These play an important role in the defence mechanism of the body. Along with monocytes, neutrophils provide the first line of defence against the invading micro-organism. Neutrophils are the free cells in the body and wander freely through the tissue and practically, no part of the body is spared by these leucocytes.

b. Eosinophils: these play an important role in the defence mechanism of the body against the parasite. During parasitic infections, there is a production of a large number of eosinophils which move towards the tissues affected by the parasite(s). Eosinophils are responsible for detoxification, disintegration and removal of foreign protein and their count increases during allergic disease conditions like asthma.

c. Basophils: The number of Basophils increases during healing conditions hence; they play an important role in the healing process of the body. Basophils also play an important role in allergy or acute hypersensitivity reaction due to the presence of receptors for immunoglobin-E (IgE) in basophile membrane.

d. Monocytes: These are the largest cells among the leucocytes. Like neutrophils, monocytes are motile (wander freely through all the tissues of the body) and phagocytic in nature i.e. play an important role in the defense of the body. Along with neutrophils, these leucocytes provide the first line of defense and secrete;

- Interleukin-1 (IL-1)
- Colony Stimulating factor (M-CFS)
- Platelet- Activating factor (PAF)

Monocytes are the precursors of the tissue macrophages because its matured cells stay in the blood only for few hours after which, the cells enter the tissues from the blood and become tissue macrophages.

e. Lymphocytes: These play an important role in immunity. Functionally, lymphocytes are classified into two categories, namely; T-lymphocytes and B-lymphocytes. T-lymphocytes are responsible for the development of cellular immunity while B-lymphocytes are responsible for the development of humoral immunity.

III. Platelets (thrombocytes): Platelets otherwise called thrombocytes are small, granulated bodies that aggregate at sites of vascular injury. They are colorless, non-nucleated, moderately refractive bodies and are formed elements of blood. They are about 300,000/μL in circulating blood, 2–4 μm in diameter and normally have a half-life of about 4 days. The **megakaryocytes** (giant cells) in the bone marrow form platelets by pinching off bits of cytoplasm and extruding them into the circulation. Between 60 and 75% of the platelets that have been extruded from the bone marrow are in the circulating blood, and the remainder are mostly in the spleen

ISSN No. 2321-2705 | DOI: 10.51244/IJRSI |Volume XII Issue II February 2025

(Barrett *et al.*, 2012; Sembulingam and Sembulingam, 2012).

Sembulingam and Sembulingam, 2012 further stated that platelets are normally of several shapes, viz; spherical or rod-shaped and become oval or disk-shaped when inactivated. Sometimes, the platelets have dumbbell shape, comma shape, cigar shape or any other unusual shape. Inactivated platelets are without processes or filopodia and the activated platelets develop processes or filopodia.

Platelets perform their functions through various substances they release. These functions as listed by **Sembulingam and Sembulingam, 2012** are;

1. Platelets are responsible for the formation of intrinsic prothrombin activator which is a substance responsible for the onset of blood clotting.

2. The cytoplasm of platelets contains contractile proteins (actin, myosin and thrombosthenin) which are responsible for clot retraction.

3. Platelets play a role in the prevention of blood loss (hemostasis) by the secretion of 5-HT, which causes the constriction of blood vessels. It also accelerates hemostasis by the formation of temporary plug and sealing the damaged/injured blood vessels like capillaries due to its adhesive property.

4. Platelet-derived growth factor (PDGF) formed in cytoplasm of platelets is useful for the repairs of the endothelium and other structures of the ruptured blood vessels.

5. Platelets encircle the foreign-bodies and destroy them by the property of agglutination.

Haematological Parameters

Haematological parameters are parameters used for assessing the effect of various substances on blood as well as the physiologic property of blood. These parameters are;

1. Red blood Cell (RBC) count
2. Haemoglobin (Hb) concentration
3. Packed cell volume (PCV)
4. Blood indices/Derived Red Blood Cell values
    - Mean Corpuscular Volume (MCV)
    - Mean Corpuscular Haemoglobin (MCH)
    - Mean Corpuscular Haemoglobin Concentration (MCHC)
    - Colour index (CI).
5. Total White Blood Cells (WBC) count
6. Differential WBCs Count
7. Platelet Count
8. Osmotic fragility

a. Red Blood Cells (RBCs) Count: Shier *et al.*, 2007 define RBCs count as the number or concentration of red blood cells in a cubic millimeter (mm^3) of blood. Although the number of RBC count varies from time to time even in healthy individuals but the typical range for adult males is 4600000-6200000 cells per mm^3, adult females

ISSN No. 2321-2705 | DOI: 10.51244/IJRSI |Volume XII Issue II February 2025

4200000-5400000 cells per mm^3 while the average range for children is 4500000-5.100000 cells per mm^3 These values may vary slightly with the hospital, physician, and type or equipment used to make blood cell counts but the number of red blood cells generally increases after several days following strenuous exercise or an increase in altitude **(Shier *et al.*, 2007).**

Given that increasing number of circulating red blood cells increases the blood's oxygen - carrying capacity, changes in this number may affect health. For this reason, red blood cell counts are routinely consulted to help diagnose and evaluate the courses of various diseases **(Shier *et al.*, 2007).** However, an increase in RBC count is known as polycythemia and it occurs in both physiological and pathological conditions. When it occurs in physiological conditions, it is called physiological polycythemia but the increase in number during this condition is marginal and temporary. Pathological polycythemia on the other hand is an abnormal increase in the RBC count i.e. usually above 7million/mm^3 **(Sembulingam and Sembulingam, 2012).**

Polycythemia is of two types; the primary polycythemia and secondary polycythemia. Primary polycythemia otherwise known as polycythemia vera is a disease characterised by persistent increase in RBC count (usually above 14million/mm^3) which usually occurs in mycloproliferative disorders like malignancy of bone marrow and typically associated with increased white blood cell count (above 24,000/mm^3 of blood). Secondary polycythemia is secondary to some of the pathological disease conditions as respiratory disorders (emphysema, congenital heart disease, Ayerza's disease - a condition associated with hypertrophy of right ventricle and obstruction of blood flow to the lungs), chronic carbon monoxide poisoning, poisoning by chemicals like phosphorus and arsenic and repeated mild haemorrhages. All these conditions lead to hypoxia which stimulates the release of erythropoietin thereby stimulating the bone marrow and causing increased RBC count **(Sembulingam and Sembulingam, 2012).**

Shier *et al.*, 2007 as well as **Sembulingam and Sembulingam (2012)** further added that decrease in RBC count also occurs in physiological (i.e. high barometric pressure, pregnancy or during sleep) and pathological conditions. Pathological decrease in RBC count is called anaemia – a blood disorder characterised by the reduction in Red blood cell (RBC) count, Haemoglobin (Hb) content and Packed cell volume (PCV) which reduces the oxygen - carrying capacity of the blood and the affected person might appear pale and lack energy. More so, reduction in the aforementioned parameters occurs due to decreased production of RBC, increased destruction of RBC and excess loss of blood from the body. All these incidents are either caused by inherited disorders, environmental influences (like nutrition & exposure to drugs or toxins) and infections.

b. Haemoglobin (HB) Concentration: Haemoglobin (Hb) is the ion containing the colouring matter of red blood cell (RBC) and its concentration can be defined as the amount of haemoglobin in blood. Haemoglobin is a chromoprotein (a protein combined with a pigment) forming about 95% of RBC's dry weight and 30-40% of wet weight **(Sembulingam and Sembulingam, 2012).**

Although, hemoglobin is necessary for the transport of oxygen and respiratory gases to the tissues, it performs another function essential to life which is; serving as a "tissue oxygen buffer" system. This implies that hemoglobin in the blood is mainly responsible for stabilizing the oxygen pressure in the tissues **(Guyton and Hall, 2006)**. It is worthy to note that the average haemoglobin (Hb) content is about 14-16g/dl and the value varies depending upon the age and sex of the individual. However, Hb concentration in adult males and females is about 15g/dl and 14.5g/dl, respectively **(Sembulingam and Sembulingam, 2012).**

c. Packed Cell Volume (PCV) or Hematocrit (HCT):

Packed cell volume (PCV) also called hematocrit (Hct) value or erythrocyte volume fraction (EVF) is the proportion of blood occupied by RBCs expressed in percentage. It is also the volume of RBCs packed at a bottom of a haematocrit tube when the blood is centrifuged. It is impossible to completely pack the red cells together; therefore, about 3-4 percent of the plasma remains entrapped among the cells and the true hematocrit is only about 96% of the measured hematocrit **(Guyton and Hall, 2006).**

Normal PCV in males is 40- 45% while in females is 38- 42% but in severe anemia, the hematocrit may fall as low as 10%, a value that is barely sufficient to sustain life. PCV increases in polycythemia, dehydration and

ISSN No. 2321-2705 | DOI: 10.51244/IJRSI |Volume XII Issue II February 2025

Dengue shock syndrome; Dengue fever (tropical disease caused by flavivirus transmitted by mosquitoes) of grade III & IV severity **(Sembulingam and Sembulingam, 2012).**

d. Derived Red Blood Cell Values

Blood indices are the calculations derived from RBC count, hemoglobin (Hb) content of blood and Packed Cell Volume (PCV). These include; Mean Corpuscular Volume (MCV), Mean Corpuscular Haemoglobin (MCH), Mean Corpuscular Haemoglobin concentration (MCHC) and Colour index (CI) **(Sembulingam and Sembulingam, 2012)**.

Mean Corpuscular Volume (MCV): MCV is the average volume of a single RBC which is expressed in cubic microns (μ^3) with a Standard value of 90μ^3 (78-90cuμ). When MCV is normal, the RBC is called normocyte; when it increases, the cell is known as macrocytes and when it decreases, it is called microcyte. In pernicious and megaloblastic anaemia, the RBCs are macrocytic in nature while in iron deficiency anaemia, the RBCs are microcytic **(Sembulingam and Sembulingam, 2012).**

Mean Corpuscular Haemoglobin (MCH): This is the quantity or amount of hemoglobin present in one RBC and is expressed in micro-microgram or picogram (pg). Normal value of MCH is between 27-32pg **(Sembulingam and Sembulingam, 2012)**.

Mean Corpuscular Haemoglobin Concentration (MCHC): This refers to the concentration of hemoglobin in one RBC or the amount of hemoglobin (in percentage) expressed in relation to the volume of one RBC. This blood index has a normal value range of 30 - 38% and is the most important absolute value in the diagnosis of anemia.

When MCHC is normal, the RBC is normochromic and when it decreases, the RBC is known as hypochromic. In pernicious anemia and megaloblastic anemia, RBCs are macrocytic and normochromic or hypochromic while in iron deficiency anemia, RBCs are microcytic and hypochromic. A single RBC cannot be hyperchromic due to the fact that the amount of hemoglobin cannot increase beyond normal **(Sembulingam and Sembulingam, 2012).**

Colour index (CI): Color index is the ratio between the percentage of hemoglobin and the percentage of RBCs in the blood. It is actually the average hemoglobin content in one cell of a patient compared to the average hemoglobin content in one cell of a normal person. Normal color index is between 0.8 - 1.2% and is useful in determining the type of anemia. However, C.I is known to be normal in normocytic normochromic anemia, increased in macrocytic (pernicious) and megaloblastic anemia and reduced in iron deficiency anemia **(Sembulingam and Sembulingam, 2012**).

It is calculated as:

Colour index = Hemoglobin %/RBC %

Where;

Hemoglobin % = Hemoglobin content in the subject/ Hemoglobin content in normal persons × 100

RBC % = RBC count in the subject/ RBC count in normal persons × 100

e. Total White Blood Cells Count (WBCC): This refers to the total number and percentages of different white blood cell types in a sample of blood. Normally, a cubic millimeter of blood includes 5,000 - 10,000 white blood cells and before a white blood cell count (WBCC or WCC) is made, the red blood cells in the blood sample are destroyed so they will not be mistaken for white blood cells. A rise in the number of circulating white blood cells may indicate infection as an increase in the total number of white blood cells (exceeding 10,000 per mm1 of blood) constitutes a disease condition known as leukocytosis; signifying acute infection like appendicitis. Leukocytosis may also follow vigorous exercise, emotional disturbances, or great loss of body fluids **(Shier *et al.*, 2007).**

ISSN No. 2321-2705 | DOI: 10.51244/IJRSI |Volume XII Issue II February 2025

Shier *et al.*, 2007 coined that a total white blood cell count below 5,000 per mm3 of blood is called leucopenia. Such a deficiency may accompany typhoid fever, influenza, measles, mumps, chickenpox, AIDS, or poliomyelitis. Leukopenia may also result from anemia or from lead, arsenic, or mercury poisoning.

f. Differential WBCs Count: A differential white blood cell count (DIFF) lists percentages of the types of leukocytes in a blood sample. This test is useful because the relative proportions of white blood cells may change in particular diseases and the number of neutrophils, for instance, usually increases during bacterial infections, and eosinophils may become more abundant during certain parasitic infections and allergic reactions.

Table 3: Table showing the normal values of cellular elements in human blood

Source: Barrett *et al.*, 2012

Cell	Cells/μL (average)	Approximate Normal Range	Percentage of Total White Cells
Total white blood cells	9000	4000–11,000	...
Granulocytes			
Neutrophils	5400	3000–6000	50–70
Eosinophils	275	150–300	1–4
Basophils	35	0–100	0.4
Lymphocytes	2750	1500–4000	20–40
Monocytes	540	300–600	2–8
Erythrocytes			
Females	4.8×10^6	...	...
Males	5.4×10^6	...	...
Platelets	300,000	200,000–500,000	...

g. PLATELET COUNT: Platelet count is the concentration of platelet in blood. Platelets ranges between 200,000 - 400,000/cu mm of blood and the normal count in blood is 250,000/cu mm. Increase in platelet count is called thrombocytosis; decrease is called thrombocytopenia while thrombocythemia is a condition with persistent and abnormal increase in platelet count which occurs in carcinoma, chronic leukemia and Hodkin's disease. However, Glanzmann's thrombasthenia is an inherited hemorrhagic disorder caused by structural or functional abnormality of platelets. It leads to thrombasthenic purpura where the platelet count is normal, clotting time is normal, bleeding time is normal or prolonged but defective clot retraction **(Sembulingam and Sembulingam, 2012).**

h. Osmotic Fragility: Osmotic fragility is one among the two types of fragility whereby the Red blood cells like other cells, shrink in solutions with an osmotic pressure greater than that of normal plasma. It occurs due to exposure to hypotonic saline and in solutions with a lower osmotic pressure the RBCs swell, become spherical rather than disk-shaped, and eventually lose their hemoglobin (hemolysis). Normal **osmotic fragility** causes red cells to hemolyze (undergo destruction and release hemoglobin) when suspended in 0.5% saline while 50% lysis (destructive disruption of cells) occurs in 0.40–0.42% saline, and complete lysis occurs in 0.35% saline **(Barrett *et al.*, 2012; Sembulingam and Sembulingam, 2012).**

However, fragility test is a test that measures the resistance of erythrocytes in hypotonic saline solution. It is done by using sodium chloride solution at different concentrations from 1.2% to 0.2%. These solutions are then taken into series of Cohn's tubes at different concentrations after which one drop of blood to be tested is added to each tube. The sodium chloride solution and the blood in each tube are then thoroughly mixed and left undisturbed for some time. Results are analyzed by directly observing the tubes or by centrifuging the tubes after 15 minutes. It should be noted that **Fragility** can be defined as the susceptibility of RBC to hemolysis or the tendency of RBC to break easily **(Sembulingam and Sembuligam, 2012).**

ISSN No. 2321-2705 | DOI: 10.51244/IJRSI |Volume XII Issue II February 2025

MATERIALS AND METHODS

Lists of Materials

1. Fifteen (15) Wistar Rats (experimental rats)
2. Animal cages
3. Cannabis *sativa*
4. Absolute ethanol (99.86%)
5. Manual grinder/blender
6. Wood beddings
7. Water troughs
8. Weighing balance
9. Chloroform anaesthesia
10. 5ml syringes
11. Dissecting sets
12. Micro-hematocrit Centrifuge
13. Oro-pharyngeal cannula
14. Ethylene-diaminetetracetate (EDTA) vials
15. Improved Neubauer Counting Chamber
16. Hayem Solution
17. Microscope
18. Microhaematocrit reader
19. Haemocytometer
20. Leishman stain (0.15% methylene azure in pure methanol)
21. Test-tubes
22. Non-heparinised sample containers
23. Refrigerator
24. Pipettes
25. Measuring cylinder
26. Spectrophotometer
27. Desiccant
28. Chemical and enzyme reagents
29. Note book
30. Calculator
31. Cheese-cloth/ sieve basket
32. Laboratory coat

Methods

Collection and preparation of Extracts: Dried leaves of Cannabis *sativa* were obtained from the Office of the National Drug Law Agency (NDLEA) Cross River State Command and were air-dried and blended into fine

ISSN No. 2321-2705 | DOI: 10.51244/IJRSI |Volume XII Issue II February 2025

powder using an electric blender. The powdered plant weighing 500g was extracted into 80% ethanol at room temperature, homogenized in a plastic container by stirring for 3 hours and thereafter, soaked and allowed in the refrigerator at 4ºc for 48 hours.

After 48 hours, the homogenate was first filtered with a sieve basket to separate the filtrate from the residue and then with cheese-cloth to remove large and small particles. A Whatman's filter paper was thereafter used to remove much smaller particles. The obtained filtrate was then concentrated at low temperature (37-40ºc) to about one tenth the original volume using a rotary evaporator and was later allowed open in a thermo-regulated water bath at a temperature of 40ºc for complete dryness.

The dry extract was placed in a refrigerator at a temperature between 2-8ºc until use. However, the weight of the crude extract was determined and recorded as 105.14g after the process.

Percentage (%) yield of Cannabis *sativa*: This is the percentage of filtrate gotten from dried weight of Cannabis *sativa* after extraction. It was calculated as thus;

Initial weight = 500g

Extract weight = 105.14g

Hence, % yield = extract weight/ Initial weight × 100/1

105.14g / 500g × 100/1

= 0.21028 × 100

= 21.028%

Preparation of Cannabis *sativa* extract for administration: 0.5g of Cannabis *sativa* extract was weighed and diluted in 50mls of normal saline and mixed until there was homogeneity. This is the same as 500mg of extract/50ml of normal saline which is 10mg/1ml. The doses were considered following LD50 report which was indicated at 30mg/kg body weight by **Benno Hartung *et al.*, (2014)**.

The mixed solution was used within 3days after which it was discarded to avoid loss of efficacy as well as atmospheric oxidation due to long exposure. This procedure was continuously repeated until the 21st day of the experiment.

Preparation of Hayem's (fluid) solution: This solution for diluting Red Blood Cells was prepared by weighing; 0**.5gms of NaCl,** 0.23gms of **$HgCl_2$** and 2.5gms of **$NaSO_4$** respectively. All these chemicals were then put in a beaker and distilled water added to make 100cc volume.

Experimental Animals

Fifteen (15) adult, male albino wistar rats weighing 200-250g were used in the study. They were obtained from the Animal house of the department of Human Physiology, Faculty of Basic Medical Sciences, University of Calabar. The animals were kept in cages lined with wood chip beddings inside a well ventilated experimental house with suitable temperature, humidity, water, normal rat chow in addition to 12hr light/dark cycle throughout the study. Their beddings were changed daily and were also allowed to acclimatise for two weeks before the study.

Feeding of the animals was diligently carried out for three (3) weeks, 21 days. But, prior to the day of euthanasia, the rats were starved for twelve (12) hours.

Experimental Procedure

This work was carried out on 3 groups of rats which comprises of 1 control group (untreated and fed with normal

ISSN No. 2321-2705 | DOI: 10.51244/IJRSI |Volume XII Issue II February 2025

rat chow and water) and 2 test groups (rats treated/administered with low and high doses of cannabis *sativa* leaf extract respectively); each group contained 5 rats and were placed in different cages for proper identification. However, all experiments on rats were carried out in absolute compliance with the University's guideline for research which also considers ethical guide for care and use of laboratory animals.

Group I- control group: The animals in this group served as control and were administered with 0.1ml/kg body weight of normal saline and were fed on normal rat chow and water ad libitum.

Group II- Low Dose (LD) group: The animals were orally administered with 100mg/kg^{-1} of Cannabis *sativa* leaf extract. The animals were also fed on normal rat chow and water ad libitum.

Group III- High Dose (HD) group: Each animal in this group was orally fed with 200mg/kg^{-1} of Cannabis *sativa* leaf extract.

Route of Administration: Administration of Cannabis *sativa* solution was done using oro-gastric feeding, with an oro-pharyngeal cannula inserted into a 1ml syringe with detachable needle. A small bead was attached to the end of the cannula to avoid injuring the animal's mouth during the process. However, the animals were first weighed and each given the solution corresponding to its body weight.

Blood sample collection: At the end of the 3 weeks feeding experiment, the animals were euthanized under chloroform anaesthesia (3.8%); the animals were dissected and blood obtained by cardiac puncture using sterile disposable 5ml syringes and needles which were disposed after use. About 3.5ml of blood was obtained from each animal into different, dried and pre-labelled centrifuge tubes containing ethylene-diaminetetracetate (EDTA). The remainder was emptied into plain tubes and allowed to clot for about two hours. Serum was separated by centrifugation for ten minutes, at 3000 revolution. The serums were stored in centrifuge tubes below -4˚c until required for analysis **(Dacie & Lewis, 2002).**

Assessment of Full Blood Count (FBC): FBC was assessed in all rats using Cell counter instrument (Coulter Electronics, Luton, Bedfordshire, UK) having standard calibrations according to the manufacturer's instruction.

Assessment of Red Blood Cell (RBCs) Count: RBC count was assessed under the principle that involves diluting a small amount of blood (1:200) with Hayem solution (that preserves the corpuscles) and the sample being counted in an improved Neubauer Counting chamber using a microscope.

Procedure: Using the methods of **Dacie & Lewis, 2001**.

This was done by sucking up 0.5mm quantity of blood from the anti-coagulant bottle containing the sample under investigation using the Red blood Cell pipette. Excess blood was wiped with tissue paper. After this, the diluting fluid was sucked from the watch glass until the mixture reached the 101mm mark. Whilst the pipette was tilted up and down between the thumb and the middle finger, the red bead in the bulk facilitated the mixing of the solutes. The stem fluid was later discarded such that the dilution of the blood was 0.5mm in (101-1) i.e. 1:200 and the pipette was then left for some time.

The Counting chamber was then cleaned and the area meant for RBC count was covered with a cover slip pressed lightly on them to show Newton's ring in a way that the distance between the lower surface of the cover slip and the surface of the counting area was 0.1mm deep. This was followed by attaching the rubber tube to the RBC pipette and the pure diluting fluid in the stem was blown out together with few drops of diluted blood. A drop of the diluted blood was thereafter introduced into the chamber by approximating the tip of the pipette to one end of the chamber. The drop ran into the chamber by capillarity and was allowed for about 5 minutes for the corpuscles to distribute evenly and settle properly. The chamber was thereafter focused with the magnification power of X40.

The rule adopted for the counting was to count all the cells that were well within the square together with those that touched the lower horizontal and left vertical lines while those that touched the upper horizontal and right vertical line were disregarded to avoid counting any cell twice. However, Red Blood Cells (RBC) were counted in 5 large squares (those of the 4 corners and one in the middle) each of which contains 16 small squares thus,

ISSN No. 2321-2705 | DOI: 10.51244/IJRSI |Volume XII Issue II February 2025

making a total of 80 small squares.

The RBC count was given as N × CF per mm^2 **(Dacie & Lewis, 2001).**

Where:

N = Total number of Cells counted in all the 5 corner squares (80 small squares)

CF = Correction factor (10,000)

Assessment of red cell absolute values (MCV, MCH and MCHC): These values were assessed using improved Neubauer counting chamber and were calculated using the formula of **Sembulingam and Sembuligam, 2012**;

1. MCV is calculated as;

MCV = PCV in mL / 1,000 mL of blood/ RBC count in million/cu mm of blood

= PCV in 1000 mL or in 100 mL/RBC count in million/cu mm × 10 cu μ

2. MCH is the quantity or amount of haemoglobin present in one RBC and is expressed in micro-microgram or picogram (pg).

MCH = Haemoglobin in gram per 1000 ml of blood/ RBC count in million/cu mm

= Haemoglobin in gram per 100 ml of blood/RBC count in million/cu mm × 10

3. **MCHC is derived by**;

MCHC = Haemoglobin in gram/100 mL of blood/PCV in 100 mL of blood × 100

Assessment of Haemoglobin (Hb) Concentration: Hb concentration of the blood was assessed based on the method by Dacie and Lewis (2001). This method is based on the fact that haemoglobin present in a sample of blood is converted to acid haematin when 0.1 normal (N) Hydrogen Chloride (HCl) is added. The Hb Concentration was determined by matching this solution against a non-fading brown colour standard and calculated as thus;

Hb content (g/dl) = (Reading (%) × 14)/ 100

Assessment of Packed Cell Volume (PCV): PCV was assessed using capillary method **(Dacie & Lewis, 2001).** The anti-coagulated blood was centrifuged and a micro-haematocrit reader was used to read the meniscus of the RBC and the PCV in percent (%).

Assessment of platelets Count: Platelets in the blood was obtained and counted using a light microscope and a haemocytometer as described by **Dacie and Lewis, 2002**. The improved Neubauer counting chamber was used for this process.

Assessment of Total White Blood Cell (TWBC) and differential WBC Count: WBCs count was assessed the same way as was described for RBC. The WBCs were identified by their nuclei which were stained by gentian violet and were counted in the 4 corner square of ruled areas of the improved Neubauer chamber using ×10 magnified lenses. The multiplication factor used was 50n

Where;

n = the number of cells counted in the four corner squares

Procedure:

Freshly prepared blood was used to determine differential count. The method that was used was as described by

ISSN No. 2321-2705 | DOI: 10.51244/IJRSI |Volume XII Issue II February 2025

Dacie and Lewis (2001) using Leishman stain (0.15% methylene azure in pure methanol). A drop of blood was placed on one slide while a second smooth-edged slide held at an angle of 45º between the thumb and forefinger was used to spread it. The smear was air-dried quickly and equal volume of buffer solution was added to the slide and mixed with the stain. The different white blood cells granulocytes (basophils, oesinophiles and neutrophils) and agranulocytes (lymphocytes and monocytes) were identified using different stains.

Statistical Analysis: The data were presented as the mean ± standard error of mean (SEM). Normally distributed data were analysed using analysis of variance (ANOVA). A value of $P<0.05$ was considered significant. All analysis were conducted using Statistical product and Service Solution (SPSS) software.

RESULTS

Effect of Normal Rat Chow on Haematological Parameters: The result in Table 1 shows that, water and normal rat chow have no effect on haematological parameters of the control and other test groups.

Effect of Cannabis Sativa Extract on Haematological Parameters: As summarised in Table 1, there was no significant increase in all the haematological indices except in the Mean Corpuscular Haemoglobin Concentration (MCHC) of animals fed with low and high doses of cannabis extract compared to the control group.

Also, there was significant decrease in Mean Corpuscular Volume (MCV) in groups of animals fed with low and high doses of cannabis *sativa* leaf extract when compared with the control group. More so, there was significant difference in MCV between the groups fed with Low Dose of Cannabis extract when compared to the High dose group.

However, there was significant increase in all the haematological parameters when compared to the control group.

The results of the experiment conducted in the previous chapter are presented here. The results analysed are specifically of haematological parameters.

Table4: Summarised Chart Showing the Effect of High and Low Doses of Cannabis Sativa Leaf Extract on Haematological Parameters Of Wistar Rats (N=5)

	Control Group	**Rats Fed With Low Dose (Ld) Of Cannabis Sativa Extract**	**Rats Fed With High Dose (Hd) Of Cannabis Sativa Extract**
Red Blood Cells (RBCs) Count	6.182 ± 0.527	7.186 ± 0.152	7.066 ± 0.312
Haemoglobin(Hb) Concentration	11.96 ± 0.496	12.86 ± 0.26	12.22 ± 0.63
Packed Cell Volume (PCV)	38.63 ± 1.801	41.19 ± 0.922	39.57 ± 1.882
Mean Corpuscular Volume(MCV)	63.38 ± 2.886	57.34 ± 0.971*	56.01 ± 1.104*
Mean Corpuscular Haemoglobin (MCH)	19.7 ± 1.211	17.9 ± 0.264	17.3 ± 0.502*
Mean Corpuscular Haemoglobin Concentration (MCHC)	31.01 ± 0.64	31.23 ± 0.22	30.86 ± 0.42

*Significant: Control group vs. Group fed with Low Dose of Cannabis extract
*Significant: Control group vs. Group fed with High dose of Cannabis extract

ISSN No. 2321-2705 | DOI: 10.51244/IJRSI |Volume XII Issue II February 2025

Table 5: Summarised chart showing Sodium Chloride (NaCl) Concentrations per Percentage (%) Haemolysis for Osmotic Fragility

	0.1	0.2	0.3	0.4	0.45	0.5	0.55	0.6	0.7	0.8	0.9	1
Control	100±0	85.2 ± 3.3971	69.6 ± 5.5911	58± 7.4632	37.4±7.4	13.6± 8.3283	4±4	0±0	0±0	0±0	0±0	0±0
Low Dose	100±0	92.8± 2.2226	82.4 ± 4.3886	74.8± 8.3271	55.6± 8.6637	31.4± 8.2982	19 *± 5.8907	2.8*± 2.3324	1.4± 1.4	0±0	0±0	0±0
High Dose	100± 0	90 ± 1.6432	83± 3.0659	67± 3.5777	54± 6.8337	36.6± 10.6189	23.4*± 7.2842	9.4 *± 4.1183	2±2	0±0	0±0	0±0

*Significant: Control group vs. Group fed with Low Dose of Cannabis extract
*Significant: Control group vs. Group fed with High dose of Cannabis extract

Osmotic Fragility:

The table above (Table 5; **Summarised chart showing Sodium Chloride (NaCl) Concentrations per Percentage (%) Haemolysis for Osmotic Fragility**) and the graph below (Figure 2; Osmotic fragility test of the different experimental groups subjected to different concentrations of NaCl) shows the Haemolytic results of the Osmotic fragility test in the Control, Low Dose and High Dose groups, respectively after being subjected to different concentrations of Sodium Chloride (NaCl) solution.

As shown in the graph (Figure 2), there was significant difference between the LD and HD groups when compared with the Control at 0.55 and 0.6 percentage NaCl Concentrations, respectively.

However, there was no statistical difference between the LD and HD at any percentage NaCl concentration as seen in Fig. 2

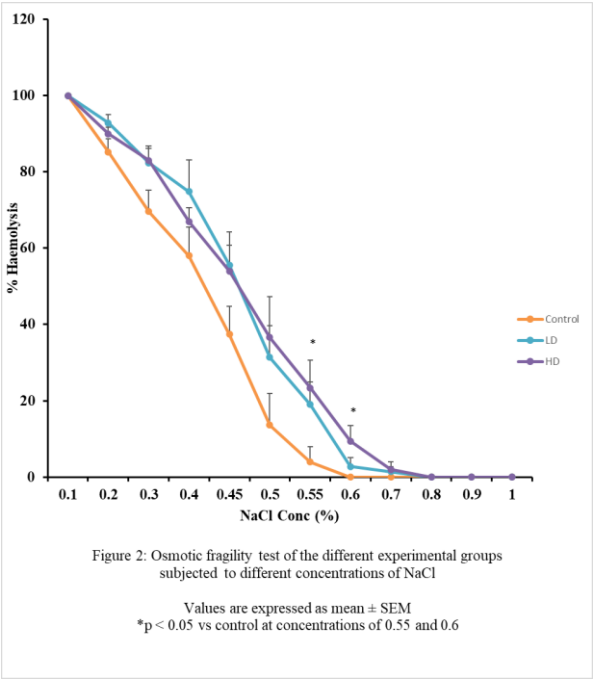


Figure 2: Osmotic fragility test of the different experimental groups subjected to different concentrations of NaCl

Values are expressed as mean ± SEM
*p < 0.05 vs control at concentrations of 0.55 and 0.6

Figure 2: Osmotic fragility test of the different experimental groups subjected to different concentrations of NaCl

Values are expressed as mean ± SEM

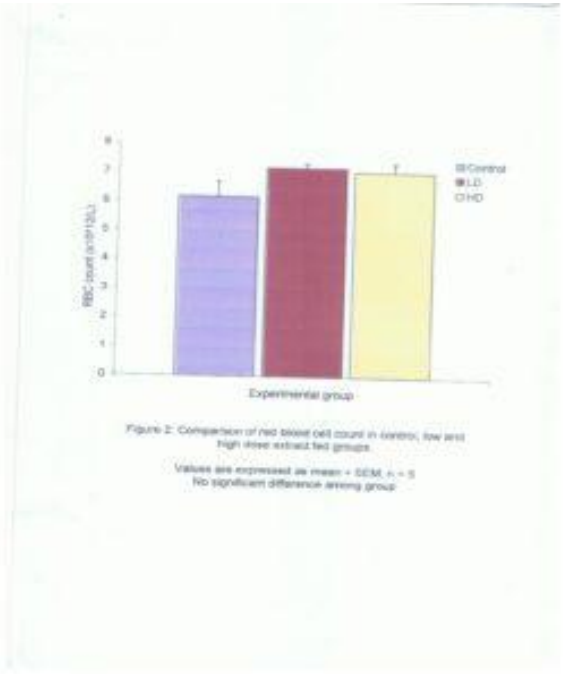
***p < 0.05 vs control at concentrations of 0.55 and 0.6**

ISSN No. 2321-2705 | DOI: 10.51244/IJRSI |Volume XII Issue II February 2025

Red Blood Cell (RBC) Count ($\times 10^{12}$/L)

The graph (Figure 3) shows the mean Red blood cell count in the three groups. RBCs counts were 6.182 ± 0.527, 7.186 ± 0.152 and 7.066 ± 0.316 for control, Low Dose (LD) and High dose (HD) of cannabis sativa extract, respectively.

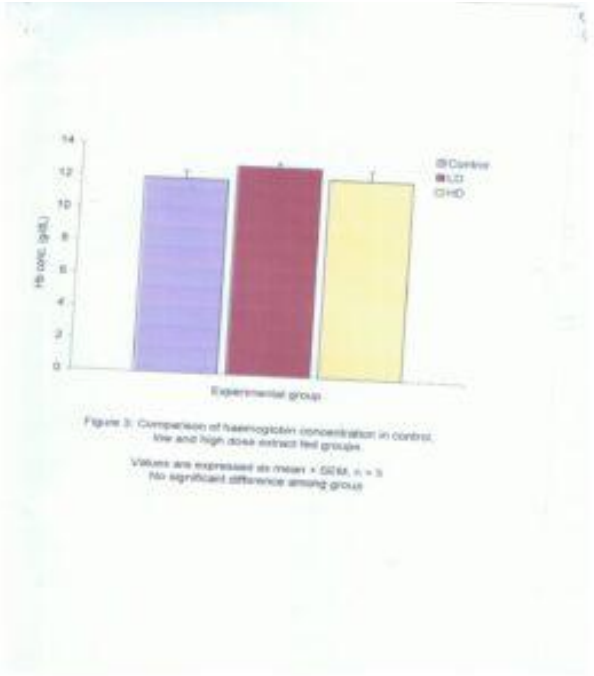
From the result shown in the table (Table 4; **summarised chart showing the effect of high and low doses of cannabis sativa leaf extract on haematological parameters of wistar rats (n=5**), there was no significant difference among the entire groups.



Haemoglobin (Hb) Concentration (g/dL):

The Haemoglobin (Hb) concentration values were 11.96 ± 0.496, 12.86 ± 0.26 and 12.22 ± 0.63 for Control, LD and HD, respectively.

There was no significant difference among the groups when compared. This is as shown in Figure 3.



ISSN No. 2321-2705 | DOI: 10.51244/IJRSI |Volume XII Issue II February 2025

Packed Cell Volume (PCV):

Packed cell volume were 38.63 ± 1.801, 41.19 ± 0.922 and 39.57 ± 1.882 for Control, LD and HD, respectively.

As seen in Table 4 and Figure 5, there was no significant difference among the groups.

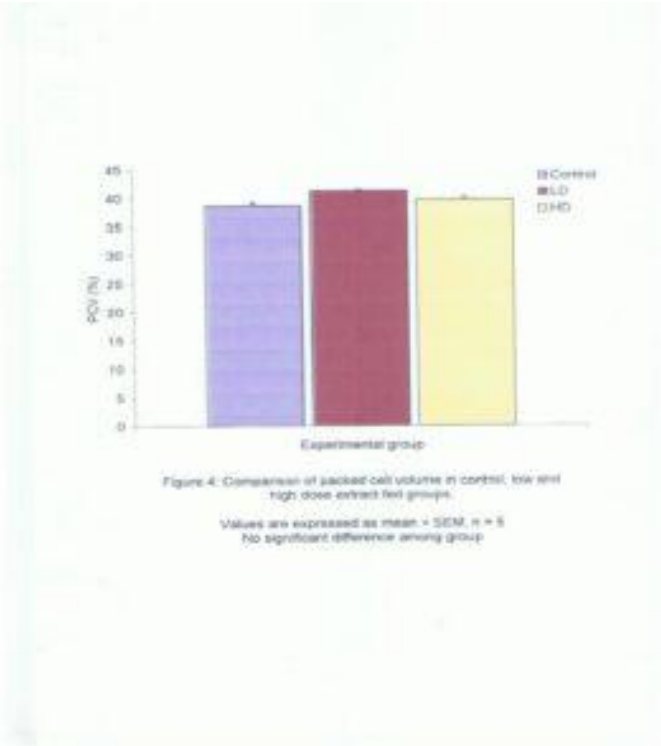


Figure 4: Comparison of packed cell volume in control, low and high dose extract fed groups.

Values are expressed as mean ± SEM, n = 5
No significant difference among group

Mean Corpuscular Volume (MCV):

The MCV levels were 63.38 ± 2.886, 57.34 ± 0.971 and 56.01 ± 1.104 for Control, LD and HD groups, respectively. The MCV in the groups of rats treated with Low and High doses of cannabis extract is observed to be significantly lower than the Control group ($P<0.05$) when compared.

There was however, no significant difference between the LD and HD groups. This is as shown in Table 4 and Fig. 6.

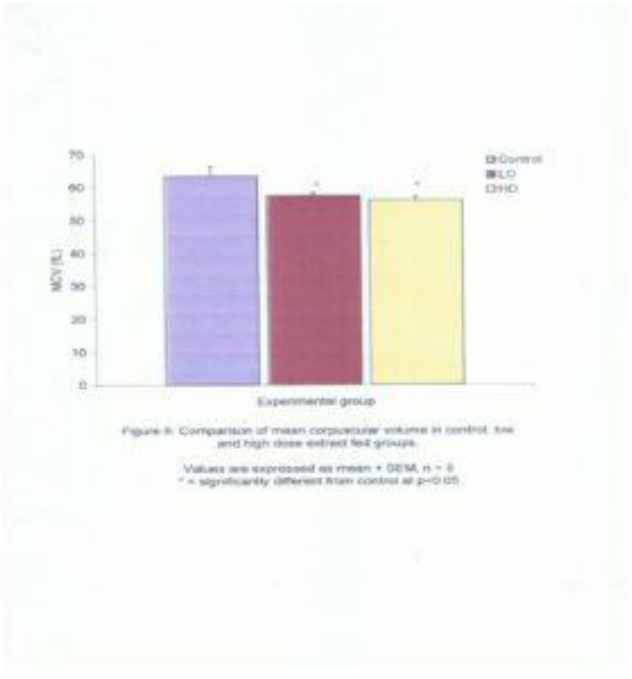


Figure 5: Comparison of mean corpuscular volume in control, low and high dose extract fed groups.

Values are expressed as mean ± SEM, n = 5
* = significantly different from control at p<0.05

ISSN No. 2321-2705 | DOI: 10.51244/IJRSI |Volume XII Issue II February 2025

Mean Corpuscular Haemoglobin (MCH):

MCH levels were 19.7 ± 1.211, 17.9 ± 0.264 and 17.3 ± 0.502 for Control, LD and H groups, respectively. The value for the group administered with High Dose of cannabis *sativa* was statistically lower than the control group ($P<0.05$) while the value for the group administered with Low Dose of Cannabis *sativa* extract showed no statistical difference when compared with the Control group (Table 4, Fig. 7).

There was also no statistical difference between the Low dose and high dose groups when compared.

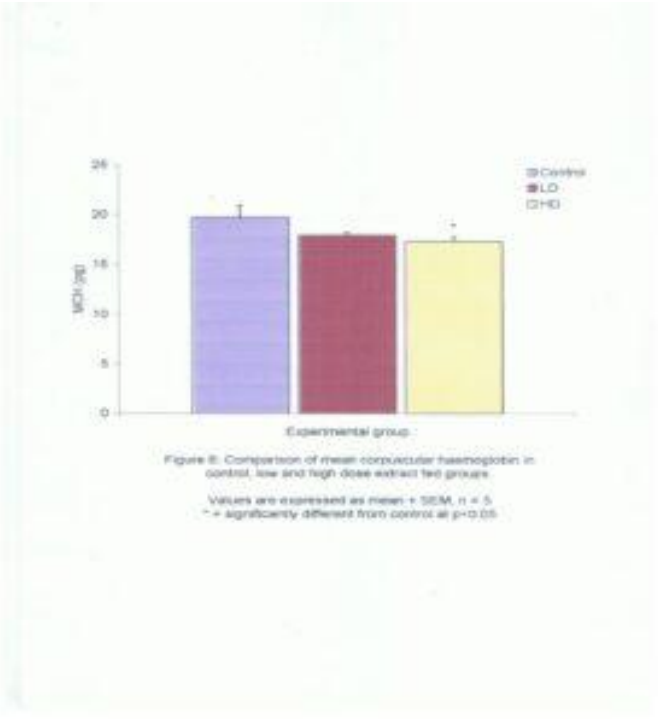


Figure 8: Comparison of mean corpuscular haemoglobin in control, low and high dose extract fed groups

Values are expressed as mean + SEM, n = 5
* = significantly different from control at p<0.05

Mean Corpuscular Haemoglobin Concentration (MCHC):

The chart (Figure 8) shows the MCHC values in the three groups of rats. MCHC levels were 31.01 ± 0.64, 31.23 ± 0.22 and 30.86 ± 0.42 for Control, Low Dose and High Dose groups, respectively.

Table 4 and Figure 8 also prove that there was no significant difference among all the groups.

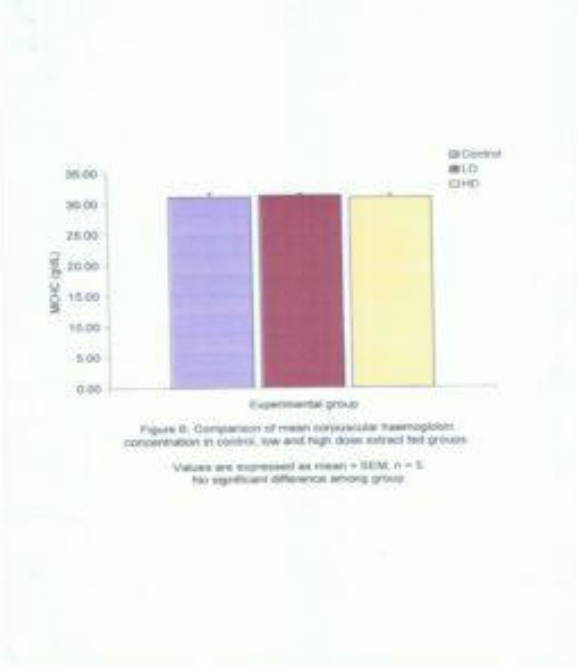


Figure 8: Comparison of mean corpuscular haemoglobin concentration in control, low and high dose extract fed groups

Values are expressed as mean + SEM, n = 5
No significant difference among group

ISSN No. 2321-2705 | DOI: 10.51244/IJRSI |Volume XII Issue II February 2025

DISCUSSION AND CONCLUSION

A valued judgment on the safety and efficacy of a particular medicinal plant and drugs can rarely be based on the results of a single study hence, pooled information is especially critical when it comes to a plant of potential importance as it is believed that over the next two decades, many useful drugs will be isolated from plants. In contrast, a combination of information indicating that a specific plant has been used in a local health care system for centuries, together with efficacy and toxicity reports by several groups of scientists, can help in deciding whether it should be considered acceptable for medicinal use **(Asati *et al.*, 2017)**. Hence, caution should be taken when consuming Cannabis *sativa* and other herbs for leisure or for therapeutic purposes.

In this study, it was seen that there was statistical difference in Osmotic Fragility of Red Blood Cells (RBCs) between the LD and HD groups when compared with the Control at 0.55 and 0.6 percentage NaCl Concentrations, respectively. Though, there was no statistical difference between the LD and HD groups at any percentage NaCl concentration. This confirms that RBC is surrounded by a semi-permeable membrane (i.e. non-distensible and not able to stretch) which when placed in a hypotonic solution would take up water, become spherical and more swollen and if the hypo-tonicity of the medium is increased, would cause the cell to hemolyze or burst **(Zafar *et al.*, 1986).**

It was also observed that the Red Blood Cell (RBC) count, Haemoglobin (Hb) concentration and Plasma Cell Volume (PCV) had no significant difference amongst the groups when compared. The result of these parameters (RBC count, Hb concentration and PCV) agrees with previous studies by **Oseni *et al.*, 2006** which showed that there was non-significant difference in the Hematological values between smokers and non-smokers of cannabis. It is therefore believed that Cannabis sativa contains Hb production-enhancing factors which may prevent the likelihood of hypochromia in Cannabis sativa treated rats **(Obembe *et al.*, 2015)**.

Reports by **Obonga *et al.*, 2005** slightly contradicted this research by stating that the erythrocytic and leucocytic counts were not significantly different in all the treated animal groups for the first two weeks of treatment but, on the third week, there was a significant increase for the groups in terms of the Packed Cell Volume (PCV), Red Blood Count (RBC), total leucocyte count, absolute lymphocyte counts, monocyte count, neutrophiles and eosinophil counts. This could be as a result of the specie, source and soil on which the cannabis was planted. However, the non-significant difference in Hb concentration in all the groups indicates that cannabis intake at a recommended dose may not impair haeme-biosynthesis during erythropoiesis and may not affect oxygen-carrying capacity of blood **(Obonga *et al.*, 2005)**.

The Mean Corpuscular Haemoglobin Concentration (MCHC) also did not show any difference between control, the low and high dose groups, respectively. However, MCHC and Mean Corpuscular Haemoglobin (MCH) is an index for diagnosing anaemia as a decrease in MCHC is an indicator of hypochromia in early iron deficiency, and MCH level decreases as the hypochromia develops **(Obembe *et al.*, 2015)**.

Low MCHC is an indicator of hypothermia in early iron deficiency, and the MCH level decreases as the hypothermia develops. It is therefore feasible that Cannabis *sativa* contains hemoglobin-production-enhancing factors. This may therefore prevent the likelihood of hypothermia in the Cannabis *sativa* treated high doses groups. Our study is in tamdem with those of **Oluwasola *et al.*, (2024)** who revealed that there were gender differences in response to Cannabis *sativa* which could be due to various factors. One of them is hormonal influences. Estrogen enhances immune responses, potentially affecting cannabis-induced immunomodulation through hormone-cannabinoid interactions. Another factor could be through cannabinoid receptor expression and signaling pathways. Cannabinoid receptors are more widely distributed in males than females. Additionally, via changing global deoxyribonucleic acid (DNA) methylation, Cannabis *sativa* may modify epigenetic changes and perhaps contribute to cannabis-induced immunosuppression, particularly on white blood cells **Oluwasola *et al.*, (2024).**

Conclusion

In conclusion, chronic consumption of Cannabis *sativa* may cause;

1. Reduced Mean Corpuscular Hemoglobin (MCH) and Mean Corpuscular Hemoglobin Concentration

ISSN No. 2321-2705 | DOI: 10.51244/IJRSI |Volume XII Issue II February 2025

(MCHC) leading to microcytic anemia.

2. Reduced white blood cell count which by implication would reduce the body's defense mechanism.

3. A non-significant difference in hemoglobin (Hb) Concentration which may not impair Oxygen-carrying capacity of blood.

Therefore, caution should be taken when cannabis and it's product is given or recommended to individuals with anaemia or immune complications.

REFERENCES

1. Adams, A. J., Brown, B., Flom, M. C., Jones, R. T. & Jampolsky, A. (1975). Alcohol and marijuana effects on static visual acuity. American Journal of Optometry and Physiological Optics, 52(11): 729-735 Retrieved from; https://www.ncbi.nlm.nih.gov/pubmed/1106208
2. Adams, A. J., Brown, B., Haegerstorm-portnoy, G., Flom, M. & Jones, R. (1976). Evidence of acute effects of alcohol and marijuana on colour discrimination. Perception & Psychophysics, 20(2): 119-124 Retrieved from; https://link.springer.com/article/10.3758/BF03199442
3. Adams, I. B. & Martins, B. R. (1996). Cannabis: pharmacology and toxicology in animals and humans. National Center for Biotechnology Information (NCBI), 91(11):1585 – 614. Retrieved from: https://www.ncbi.nlm.nih.gov/pubmed/8972919
4. Akpaso, M. I., Atangwho, I. J., Akpantah, A., Fischer, V. A., Igiri, A. O. & Ebong, P. E. (2011). Effect of combined leaf extracts of Vernonia amygdalina (bitter leaf) and Gongronema latifolium (utazi) on the pancreatic β-cells of Streptozocin induced diabetic rats. British Journal of medicine & medical research, 1(1): 24-34
5. Amaza, D. S., Maidugu, F. A., Zirahei, J. V., Numen, A. I. & Mari, H. (2013). The effect of Cannabis sativa leaves aqueous extract on cerebral cortex in albino rats. IOSR Journal of Dental and medical Science 6(2): 52-58. Retrieved from: www.iosrjournals.org
6. Amna, H., Mukhtar, M. & Nabiela, M. E. (2011). Effect of cannabis sativa on haematological indices in rats and men. Pakistan Journal of Nutrition, 10(4): 313-316 ISNN 1680-5194
7. Asati, A. K., Sahoo, H. B., Sahu, S. & Dwivedi, A. (2017). Phytochemical and Pharmacological profile of Cannabis sativa L. International Journal of Indigenous Herbs and Drugs, 2(2): 37-45
8. Asch, R. H., Fernandez, E. O., Smith, C. G. & Pauerstein, C. J. (1979). Pre-coital single doses of Avicenna: a canon of medicine, 1999; Book 3, part 1 p. 65
9. Ashton, C. H. (2011). Pharmacology and effects of Cannabis: a brief review. British Journal of Psychiatry 178 (2): 1010 - 1016
10. Audu, B. S., Ofojekwu, P. C., Ujah, A. & Ajima, M. N. O. (2014). Phytochemical, proximate composition, amino acid profile and characterization of Marijuana (*Cannabis sativa* L.). The Journal of Phytopharmacology 3(1): 35-43 Retrieved from: www.phytopharmajournal.com
11. Barrett, K. E., Barrman, S. M., Boitano, S. & Brooks, H. L. (2012). Ganong's review of Medical Physiology, 24th edition. Boston: Mc Graw Hill p.555-570
12. Barsky, S. H., Roth, M. D., Kleerup, E. C., Simmons, M. & Tashkin, D. P. (1998). Histopathologic and Molecular Alterations in Bronchial Epithelium in Habitual Smokers of Marijuana, Cocaine, and/or Tobacco. *Journal of the National Cancer Institute*, 90(16): 1198–1205 Retrieved from; https://doi.org/10.1093/jnci/90.16.1198
13. BBC News (2012). Crackdown on Marijuana in California. 23rd September, 2012 Retrieved from; https://www.bbc.com/news/av/world-us.../crackdown-on-marijuana-in-california
14. Benson, M. & Bently, A. M. (1995). Lung disease induced by drug addiction. Thorax, 50(11): 1125-1128 Retrieved From; https://www.ncbi.nlm.nih.gov/pmc/articles/PMC475080/
15. Blows, S., Ivers, R. Q., Connor, J., Ameratunga, S., Woodward, M. & Norton, R. (2005). Cannabis use and car crash injury. Addiction, 100(5): 605-611 Retrieved from; https://www.ncbi.nlm.nih.gov/pubmed/15847617
16. Borrelli, F., Aviello, G., Romano, B., Izzo, A., Orlando, P., Cappasso, R., Maiello, F., Guadagno, F., Petrosino, S. & DiMarzo, V. (2009). Cannabidiol, a safe and non-psychotropic ingredient of the marijuana plant Cannabis sativa, is protective in a murine model of colitis. Journal of Molecular

Medicine, 87(11): 1111-1121 Retrieved from; https://www.researchgate.net/.../26751588_Cannabidiol_a_safe_and_non-psychotropic
17. Bosker, W. M., Theunissen, E. L., Conen, S., Kuypers, K. P., Jeffery, W. K., Walls, H. C., Kauert, G. F., Toennes, S. W., Moeller, M. R. & Ramaekers, J. G. (2012). A placebo-controlled study to assess standardized field sobriety tests performance during alcohol and cannabis intoxication in heavy cannabis users and accuracy of point of collection testing devices for detecting THC in oral fluid. Psychopharmacology (Berl), 223(4): 439-446 Retrieved from; https://www.researchgate.net/.../224950639_A_placebo-controlled_study_to_assess_Sta... PDF
18. British Medical Association (1997). Therapeutic uses of Cannabis. London: Harwood Academic
19. Bromley, B. & Zimmerman, E. (1976). Divergent release of prolactin and corticosterone following Delta-9-THC injection in male rats. Federation of American Society for Experimental Biology journal 35 p. 220
20. Budney, A. J. & Hughes, J. R. (2006). The Cannabis withdrawal syndrome. Current Opinion in Psychiatry, 19(3): 233-238
21. Busto, U., Bendayan, R. & Sellers, E. M. (1989). Clinical pharmacokinetics of non-opiate abused drugs. Clinical Pharmacokinetics 16(1): 1-26 Retrieved from; https://link.springer.com/article/10.2165%2F00003088-198916010-00001
22. Capasso, R., Borrelli, F., Aviello, G., Romano, B., Scalisi, C. & Capasso, F. (2008). Cannabidiol, extracted from Cannabis sativa, selectively inhibits inflammatory hypermotility in mice. British Journal of Pharmacology, 154(5): 1001-1008 Retrieved from; https://doi.org/10.1038/bjp.2008.177
23. Capasso, R., Borrelli, F., Casio, M. G., Aviello, G., Huben, K., Zjawiony, J. K., Marini, P., Romano, B., Di Marzo, V., Capasso, F. & Izzo, A. A. (2008). Inhibitory effect of salvinorin A, from Salvia divinorum, on ileitis-induced hypermotility: cross-talk between kappa-opioid and cannabinoid CB1 receptors. British Journal of Pharmacology (2008), 115: 681-689 Retrieved from; https://pdfs.semanticscholar.org/ e103/2b01816b9b7c7866eb08f58d3246595a0fc2.pdf
24. Carlini, E. A. & Cunha, J. M. (1981). Hypnotic and antiepileptic effects of Cannabidiol. Journal of Clinical Pharmacology, 21(S1): 417S-427S Retrieved from; https://accp1.onlinelibrary.wiley.com/doi/abs/10.1002/j.1552-4604.1981.tb02622.x
25. Cates, W. & Pope, J. N. (1977). Gynecomastia and cannabis smoking: a non-association among U.S Army soldiers. American Journal of Surgery, 134: 613-615
26. Centers for Disease Control and Prevention (CDC), (2017). Marijuana and Public Health Retrieved from: https://www.cdc.gov/marijuana/health-effects.htm
27. Chase, P. B., Hawkins, J., Mosier, J., Jimenez, E., Boesen, K., Logan, B.K., & Walter, F. G. (2016). "Differential Physiological and Behavioral Cues Observed in Individuals Smoking Botanical Marijuana versus Synthetic Cannabinoid Drugs", Clinical Toxicology, 54(1): 14-19
28. Chusid, M. J., Gelfand, J. A., Nutter, C. & Fauci, A. S. (1975). Pulmonary aspergillosis, inhalation of contaminated marijuana smoke, chronic granulomatous disease. Annals of Internal Medicine, 82(5): 682-683 Retrieved from; https://www.ncbi.nlm.nih.gov/pubmed/1094876
29. Citak, K., Roberts, B. & Iwai, M. (2012). Effects of cannabis intoxication on eye movements and other physiological indicators. American Academy of Optometry; 2012 Abstract Retrieved from; http://www.aaopt.org
30. Coates, R. A., Farewell, V. T., Raboud, J., Read, S. E., Macfadden, D. K., Calzavara, L. M., Johnson, J. K., Shepherd, F. A. & Fanning, M. M. (1990). Cofactors of progression to acquired immunodeficiency syndrome in a cohort of male sexual contacts of men with human immunodeficiency virus disease. American Journal of Epidemology. 132(4): 717-722 Retrieved from; https://doi.org/10.1093/oxfordjournals.aje.a115713
31. Cone, E. (1986). Acute effects of marijuana on hormones, subjective effects and performance in male human subjects, Pharmacology, Biochemistry and Behaviour. Science Direct, 24 (6): 1749-1754 Retrieved from; https://www.sciencedirect.com/science/article/pii/0091305786905150
32. Costa, B. (2007). The pharmacological properties of Delta9-tetrahydrocannabinol (THC). Chemistry and Biodiversity; 4(8): 1664-1677
33. Crean, R. D., Crane, N. A. & Mason, B. J. (2011). An evidence based review of acute and long-term effects of Cannabis use on executive cognitive functions. Journal of Addict Med 5(1): 1-8
34. Crippa, J. A., Derenusson, G. N., Chagas, M. H., Atakan, Z., Martin-Santos, R., Zuardi, A. W. & Hallak,

J. E. (2012). Pharmacological interventions in the treatment of the acute effects of cannabis; a systemic review of literature. Harm Reduction Journal, 9(1): 7
35. Dacie, J. V. & Lewis, S. M. (2001). Practical Haematology. London: Churchill Living Stone p. 58-72
36. Dasilva, M. A., Grieve, K. L., Cudeiro, J. & Rivadulla, C. (2012). Endocannabinoid CB1 receptors modulate visual output from the thalamus. Psycopharmacology (Berl), 219(3): 835-845 Retrieved from; https://www.ncbi.nlm.nih.gov/pubmed/21773721
37. Dawson, W. W., Jimenez-Antillon, C. F., Perez, J. M. & Zeskind, J. A. (1997). Marijuana and vision after ten years' use in Costa Rica. Invest Ophthalmol Vis Sci, 16(8): 689-699
38. Devane, W. A., Dysarz, F. A., Johnson, M. R., Melvin, L. S. & Howlett, A. C. (1988). Determination
39. and characterisation of a cannabiniod receptor in rat brain. Mol Pharmacol, 34:605
40. Devane, W. A., Hanus, L. & Breuer, A. (1992). Isolation and structure of a brain constituent that binds to the cannabinoid receptor. Science, 258 p. 1946-1949
41. Di Carlo, G. & Izzo, A. A. (2003). Cannabinoids for gastrointestinal diseases: potential therapeutic application. Expert Opinion on investigational drugs, 12(1): 39-49 Retrieved from; https://pdfs.semanticscholar.org/e4be/aacd28968082f865166b01c15a93903bf47f.pdf
42. Dixit, V. P., Arya, M. & Lohiya, N. K. (1975). The effect of chronically administered cannabis extract on the female genital tract of mice and rats. Endokrinologie 66(3): 365-368
43. Dixit, V. P., Gupta, C. L. & Agarwal, M. (1977). Testicular degeneration and narcosis induced by chronic administration of cannabis extract in dogs. Endokrinologie 69: 299-305
44. Duke, J. A. (1983). Hand book of energy crops; emphasis on man. Purdue University, United States. Pharmacological reviews 38: 21 – 43
45. Eledo, B. O., Dioka, C. E., Amilo, G. I., Ifeanyichukwu, M. O. & Onuoha, E. C. (2015). Evaluation of some haematological parameters among marijuana smokers in Yenegoa, Nigeria. Journal of Biology, Agriculture and Health care, 5(12): 103-108 Retrieved from; www.iiste.org/Journals/index.php/JBAH /article/download/23272/24023
46. European Monitoring Centre for Drugs and Drug addiction (EMCDDA) - Annual report, (2012). The state of the drugs problems in Europe, Luxembourg: Publication Office of the European Union 2012
47. Fabre, L. F. & McLendon, D. (1981). The efficacy and safety of nabilone (a synthetic cannabinoid) in the treatment of anxiety. Journal of Clinical Pharmacology, 21(S1): 377S-382S
48. Fisk, J. E. & Montgomery, C. (2008). Real-world memory and executive processes in cannabis users and non-users. Journal of Psychopharmacology, 22(7): 727-736
49. Foltrin, R. W., Fischman, M. W. & Byrne, M. F. (1988). Effects of smoked marijuana on food intake and body weight of humans living in a residential laboratory. Appetite 11(1): 1-14
50. Gardner, E. L. (1992). Cannabiniod interaction with brain reward systems – The neurological basis of cannabinoid abuse. IN: Murphy, L. & Bartke, A. (1992). Marijuana/Cannabinoids: Neurobiology and Neurophysiology. Boca Raton: CRC press p. 275-336
51. Gold, M. S. (1991). Marijuana, In: Miller, N. S.(ed). Comprehensive handbook of alcohol and drug addiction. New York: Marcel Dekkel Inc. P. 353-376
52. Graham, T. (1998). Fertility complications due to drug intake. British Journal of fertility 189: 204-210
53. Grant, J., Chamberlain, S., Schreiber, L. & Odlaug, B. (2012). Neuropsychological deficits associated with Cannabis use in young adults. Drug Alcohol Depend 121(1-2): 159-162
54. Grégorio, C., Lichtfouse, E., Chanet, G. & Crini, N. (2020). Applications of hemp in textiles, paper industry, insulation and building materials, horticulture, animal nutrition, food and beverages, nutraceuticals, cosmetics and hygiene, medicine, agrochemistry, energy production and environment: a review. *Environmental Chemistry Letters*, 18(3): 1451–1476. DOI:10.1007/s10311-020-01029-2. Retrived from: https://www.researchgate.net/publication/342021371_Applications_of_hemp_in_textiles_paper_industry_insulation_and_building_materials_horticulture_animal_nutrition_food_and_beverages_nutraceuticals_cosmetics_and_hygiene_medicine_agrochemistry_energy_pr/citations
55. Greydanus, D. E., Feucht, C. L. & Hawver, E. K. (2012). Substance abuse disorder. In: Greydanus, D. E., Patel, D. R., Omar, H. A, Feucht, C. & Merrick, J. (eds). Adolescent Medicine: Pharmacotherapeutics in General, Mental and sexual Health. Berlin: De Gruyter p.157-199
56. Grotenhermen, F. & Russo, E. (eds). (2002). Cannabis and cannabinoids; Pharmacology, Toxicology and Therapeutic potential. New York: The Haworth press p. 181-195 Retrieved from; https://books.google.com.ng/books?isbn=113661494X

ISSN No. 2321-2705 | DOI: 10.51244/IJRSI |Volume XII Issue II February 2025

57. Grotenhermen, F. (2003). Pharmacokinetics and pharmacodynamics of cannabinoids. Clinical pharmacokinet 42: 327-360 Retrieved from; https://www.researchgate.net/publication/10846458
58. Grotenhermen, F. (2004). Pharmacology of cannabinoids. Neuroendocrinology letters 25(1-2): 14-23 Retrieved from: nel.edu/grotenhermen-11163
59. Guyton, A. C. & Hall, J. E. (2006). Textbook of Medical Physiology, eleventh edition. Pennsylvania: Elsevier Saunders p. 417-468
60. Hall, J. E. (2011). Guyton and Hall: textbook of medical Physiology, twelfth edition. New Delhi: Elsevier p. 417-438
61. Hall, W. & Degenhardt, L. (2009). Adverse health effects of non-medical cannabis use. Lancet, 374(2): 1383-1391
62. Hall, W. & Solowij, N. (1998). Adverse effects of Cannabis. The Lancet, 352(9140): 1611 – 1615 Retrieved from; https://www.sciencedirect.com/science/article/pii/S0140673698050211
63. Hall, W., Degenhardt, L. & Lynskey, M. (2001). The health and psychological consequences of cannabis use; Monograph series no. 44, 2nd edition. Commonwealth of Australia: National Drug and Alcohol Research Centre p.31-36 Retrieved from; www.drugpoint.org.au/drugs...effects/cannabis/The_health_%20and_psychological_e...
64. Hamann, W. & Divadi, P. P. (1999). Analgesic effect of the cannabinoid analogue nabilone is not mediated by opioid receptors. Lancet 1999; 353:560-572
65. Harmon, J. & Aliapoulios, M. A. (1972). Gynecomastia in marijuana users. New England Journal of Medicine 287(18): 936-942
66. Hartung, B., Kauferstein, S., Ritz-Timme, S. & Daldrup, T. (2014). Sudden unexpected death under acute influence of cannabis. Forensic Science International, 237: 11-13
67. Hazekamp, A., Ruhaak, R., Zuurman, L., Gerven, J. V. & Verpoorte, R. (2006). Evaluation of a vaporizing device (Volcano) for the pulmonary administration of tetrahydrocannabinol. Journal of Pharmacological Science, 95(6): 1308-1317 Retrieved from; https://onlinelibrary.wiley.com/doi/abs/10.1002/jps.20574
68. Hembree, W. C., Zeidenberg, P. & Nahas, G. G. (1976). Marihuana's effect on human gonadal function in: Nahas, G. G. (ed.). Marihuana: Chemistry, Biochemistry and Cellular effects. New York: Springer-Verlag p. 52
69. Herkenham, M. (1995).Localization of cannabinoid receptors in brain and periphery, IN: Pertwee, R. (ed). Cannabinoid receptors. New York: Academic Press p. 145-166
70. Hollister, L. E. (1986). Aspects of Cannabis. Pharmacological reviews, Mar; 38(1): 1-20 Retrieved from; https://www.ncbi.nlm.nih.gov/pubmed/3520605
71. Hser, Y. I., Kagihara, J., Huang, D., Evans, E. & Messina, N. (2012). Mortality among substance-using mothers in California: a 10-year prospective study. Addiction 107(1): 215-222
72. Huestis, M. A., Hermingfield, J. E. & Cone, E. J. (1992a). Blood cannabis1: absorption of THC and formation of 11-OH-THC and THC-COOH during and after marijuana smoking. Journal of Anatomy and Toxicology, 16(5): 276-282
73. Huestis, M. A., Sampson, A. H., Holicky, B. J., Henningheld, J. E. & Cone, E. J. (1992b). Characterization of the absorption phase of marijuana smoking. Clinical Pharmacology and Therapeutics, 52: 31-41
74. Hunt, R. H. & Tougas, G. (2002). Evolving concepts in functional gastrointestinal disorders: promising directions for novel pharmaceutical treatments. Best Practice & Research in Clinical gastroenterology, 16(6): 869-883
75. Inderbir, S. (2006). Human Histology, 5th edition. New Delhi: Jaypee brothers p. 74-78. ISBN: 81-8061-809-9
76. Iversen, L. (2005). Long-term effects of exposure to Cannabis. Current Opinion in Pharmacology 5(1): 69-72 Retrieved from; cannabiscoalition.ca/info/IversenCannabisEffects.pdf
77. Izzo, A. A., Mascolo, N. & Capasso, F. (2000). Forgotten target for marijuana: The endocannabinoid system in the gut. Trends Pharmacological science, 21(10): 372-373
78. Izzo, A. A., Mascolo, N. & Capasso, F. (2001). The gastrointestinal pharmacology of cannabinoids. Current Opinion in Pharmacology. 1(6): 597-603
79. Johns, A. (2001). Psychiatric effects of Cannabis. British Journal of Psychiatry, 178(2): 116-122 Retrieved from; https://www.cambridge.org/...psychiatry/.../psychiatric-effects-of-

cannabis/08CDBE0B
80. Johnson, B. A. (1990). Psychopharmacological effects of Cannabis. British Journal of Hospital Medicine 43(2): 114-116, 118-1220 Retrieved from; https://www.researchgate.net/publication/20976768 _Psychopharmacological_effects_of_cannabis
81. Karimi, I., Havatghaibi, H., Yousefi, J., Saberivand, A. & Zavareh, S. (2007). The Effect of Cannabis sativa L. (Hemp Seed) on Hematological Parameters in Guinea Pigs. Benthem Science Publishers 7(4): 288-290. Retrieved from: http://www.eurekaselect.com/65959: DOI: 10.2174/187152907782793554
82. Kochar, M. S. & Hosko, M. J. (1973). Electrocardiographic effects of marihuana. JAMA Network, 225(1): 25-28 Retrieved from; https://jamanetwork.com/journals/jama/fullarticle/349199
83. Kolodny, R. C., Masters, W. H., Kolodner, R. M. & Toro, G. I. (1974). Depression of plasma testosterone
levels after chronic intensive marijuana use. New England Journal of Medicine, 872: 872-874
84. Korantzopoulos, P. (2014). Marijuana smoking is associated with atrial fibrillation. American Journal of Cardiology 113(6): 1084-1086
85. Leung, L. (2011). Cannabis and it's derivatives; review of medical use. Journal of the American Board of Family Medicine, 24(4): 452-462. Retrieved from: doi:3122/jamfm.2011.04.100280.J.AM.board .fam.med/July-August
86. Malinowska, B., Baranowska-Kuczko, M. & Schlicker, E. (2012). Triphasic blood pressure responses to Cannabinoids: do we understand the mechanism? British Journal of Pharmacology; 165(7): 2073-2088. Doi:1
87. Martin, B. R. (1995). Marijuana, IN: Bloom, F. E., Kupfer, D. J. (eds). Psychopharmacology; the fourth generation of progress. New York: Raven press p. 1757-1765
88. Martin-Santos, R., Crippa, J. & Batalla, A. (2012). Acute effects of a single, oral dose of Δ9-tetrahydrocannabinol (THC) and Cannabidiol (CBD) administration in healthy volunteers. Current Pharmaceutical Design, 18(32):4996-4999
89. Matsuda, L. A., Lolait, S. J., Brownstein, M. J., Young, A. C. & Bonner, T. I. (1990). Structure of cannabinoid receptor and functional expression of the cloned c DNA. Nature, 346 p.561
90. Maykut, M. O. (1985). Health consequences of acute and chronic marihuana use. Progress in Neuro-psychopharmacology and Biological Psychiatry 9(3): 209 – 238
91. McIsaac, W. M., Fritchie, G. E., Idanpaan-Heikkila, J. E. & Englert, L. K. (1971). Distribution of marijuana in monkey brain and concomitant behavioural effects. Nature; 230: 593 - 595
92. Mckim, W. A. (2002). Drugs and Behaviour: an introduction to behavior pharmacology, 5th edition. New York: Prentice Hall. ISBN 0-13-048118-1
93. Meier, M. H., Caspi, A., Ambler, A., Harrington, H., Houts, R. & Keefe, R. S. (2012). Persistent cannabis users show neuropsychological decline from childhood to midlife. Proceedings of the National Academy of Sciences of the USA – PNAS, 109(40): E2657-E2664 Retrieved from; http://www.pnas.org/content /109/40/E2657
94. Mendelson, J. H. & Mello, N. K. (1984). Effects of marijuana on neuro-endocrine hormones in human males and females in: Braude, M. C., Ludford, J. P. (eds). Marijuana effects on the endocrine and reproductive systems. Washington: Government Printing Office p. 97-109
95. Mendelson, J. H., Cristofaro, P., Ellingboe, J., Benedict, R. & Mello, N. K. (1985). Acute effects of marihuana on Luteinizing hormone in menopausal women. Pharmacology, Biochemistry and Behavior 23(5): 765-768
96. Mendelson, J. H., Kuehnle, J., Ellingboe, J. & Barbor, T. (1974). Plasma testosterone levels before, during and after chronic marijuana smoking. New England Journal of Medicine 291(20): 1051-1055
97. Mendelson, J. H., Mello, N. K., Ellingboe, J., Skupny, A. S. T., Lex, B. W. & Griffin, M. (1986). Marihuana smoking suppresses Luteinizing hormone in women. The Journal of Pharmacology and Experimental Therapeutics, 237(3): 862-866
98. Merzouki, A., Ed-derfoufi, F., & Molera, J. (2000). Hemp (Cannabis sativa L.) and abortion. Journal of Ethnopharmacology 73(3): 501-503
99. Mittleman, M. A., Lewis, R. A., Maclure, M., Sherwood, J. B. & Muller, J. E. (2001). Triggering myocardial infarction by marijuana. Circulation 103(23): 2805-2809
100. Montgomery, C., Seddon, A. L., Fisk, J. E., Murphy, P. N. & Jansari, A. (2012). Cannabis-related deficits in real-world memory. Human Psychopharmacology, 27(2): 217-225

101. Morrison, P. D., Zois, V., Mckeown, D. A., Lee T. D., Hoel, D. W., Powell, J. F., Kapur, S. & Murray, R. M. (2009). The acute effects of synthetic intravenous Δ9- tetrahydrocannabinol on psychosis and mood and cognitive functioning. Psychopharmacological Medicine, 39: 1607-1616
102. Mueller, B. A., Daling, J. R., Weiss, N. S. & Moore, D. E. (1990). Recreational drug use and the risk of primary infertility. Epidemology 1(3): 195-200
103. Mukhtar, A. H & Elbagir, N. M. (2011). Effects of Cannabis sativa on haematological indices in rats and men. Pakistan journal of Nutrition 10(4): 313-316. Retrieved from: http://Scialert.net/qredirect.php?doi
104. Musty, R. E., Reggio, P. & Consroe, P. (1995). A review of recent advances in cannabinoid research and the 1994 international symposium on cannabis and the cannabinoids. Life Science, 56 p. 1933-1940
105. Nath, D., Sethi, N., Srivastava, S., Jain, A. K. & Srivastava, R. (1997). Survey on indigenous medicinal plants used for abortion in some districts of Uttar Pradesh. Fitoterapia 68(3): 223-225
106. Nir, I., Ayalon, D., Tsafriri, A. (1973). Suppression of cyclic surge of Luteinizing hormone secretion and of ovulation in the rat by THC. Nature 243: 470-471
107. Noyes, R., Brunk, S. F., Baram, D. A. & Baram, A. (1975). The analgesic properties of delta-9-tetrahydrocannabinol. Journal of Clinical Pharmacology 15(2): 139-143
108. Nwangwa, E. K., Arigi, Q. E., Naiho, A. O. & Jeroh, E. (2008). The effect of Cannabis sativa on testosterone level and seminal fluid analysis of male wistar rats. Current World Environment 3(2): 223-226, Retrieved from; www.cwejournal.org/pdf/vol3no2/CWEVO3NO2P223-226.pdf
109. Obembe, A. O., Omini, G. C., Okon, U. A., Okpo-ene, A. I. & Ikpi, D. E. (2015). Haematological and Immunological Effect of Cannabis sativa on Albino Wistar Rats. British Journal of Medicine & Medical Research 7(1): 52-60 ISSN: 2231-0614, Retrieved from; DOI: 10.9734/BJMMR/2015/15201
110. Obonga, W. O., Osadebe, P. O., Esimone, C. O. & Ihedioha, J. (2005). Haematotoxic Evaluation Of Crude Cannabis Resin In Rats. Journal of Pharmaceutical and Allied Sciences 3(1): (2005) 278 – 282 Retrieved from; DOI: 10.4314/jophas.v3i1.34991
111. Oguwike, F. N., Ukekwe, F. I., Onubeze, D. P., Ebede, S. O. & Chiaumba, T. K. (2016). Efficacious effect of Cannabis sativa (Indian hemp) on Cutanous wound healing and its haemostatic and chemical profile in adult male albino wistar rat. Greener Journal of Medical Sciences 1 p.10-17
112. Oseni, B. S., Togun, V. A. & Taiwo, O. F. (2006). Effect of Marijuana smoking on some haematological parameters of smokers. World Journal of Medical Sciences 1(2): 82-85
113. Pertwee, R. G. (1995). Pharmacological, Physiological and clinical implications of the discovery of cannabinoid receptors: an overview. New York: Academic press p. 1-34
114. Petro, D. J. & Ellenberger, C. (1981). Treatment of human spasticity with Δ9-tetrahydrocannabinol. Journal of Clinical Pharmacology, 21(S1): 413S-416S from; https://www.researchgate.net/.../675 1301_The_treatment...
115. Plant For A Future (PFAF), (2017). Cannabis sativa Hemp, Marijuana PFAF plant database. Retrieved from: www.pfaf.org/user/Plant.aspx?LatinName=Cannabis+sativa
116. Polen, M. R., Sidney, S., Tekawa, I. S., Sadler, M. & Friedman, G. D. (1993). Health care use by frequent marijuana smokers who do not smoke tobacco. Western Journal of Medicine, 158(6): 596-601 Retrieved from; https://www.ncbi.nlm.nih.gov/pubmed/8337854
117. Pope, H. G. (Jr.), Gruber, A. J. & Yurgelun-Todd, D. (2001). Residual neuropsychologic effects of Cannabis. Currrent Psychiatry Reports 3(6): 507-512 Retrieved from; https://link.springer.com/article/10.1007/s11920-001-0045-7
118. Pope, H. G. (Jr.), Gruber, A. J., Hudson, J. I., Cohane, G., Huestis, M. A. & Yurgelun-Todd, D. (2003). Early-onset of cannabis use and cognitive deficits: what is the nature of the association? Drug Alcohol Depend 69(3): 303-310
119. Pope, H. G. (Jr.), Gruber, A. J., Hudson, J. I., Huestis, M. A. & Yurgelun-Todd, D. (2002). Cognitive measures in long-term Cannabis users. Journal of Clinical Pharmacology 42(11): 41S-47S
120. Rettori, V., Wenger, T., Snyder, G., Dalterio, S. McCann, S. M. (1988). Hypothalamic action of Delta-9-tetrahydrocannabinol to inhibit the release of prolactin and growth hormone in the rat. Neuroendocrinology 47: 498-503
121. Rod, R. S., Trent, D. & Philip, T. (1992). Anatomy and Physiology, 2nd edition. Mosby: Pp 585-595 ISBN 0-8016-4832-7
122. Romano, E. & Voas, R. B. (2011). Drug and alcohol involvement in four types of fatal crashes. Journal

of Studies on Alcohol and drugs.
123. Ryan, K. S., Bash, J. C., Hanna, C. B., Hedges, J. C., & Lo, J. O. (2021). Effects of marijuana on reproductive health: preconception and gestational effects. *Current opinion in endocrinology, diabetes, and obesity*, *28*(6), 558–565. https://doi.org/10.1097/MED.0000000000000686. Retrieved from: https://pmc.ncbi.nlm.nih.gov/articles/PMC8580253/
124. Sailani, M. R. & Moeini, H. (2007). Effect of *Ruta graveolens* and *Cannabis sativa* alcoholic extract on spermatogenesis in the adult wistar male rats. Indian Journal of Urology 23: 257 - 260
125. Schuber, M. (2008). Effect of Cannabinoid receptors against rat gastric acid secretions, disrupture estream invitus and invivos. Digestive Diseases and Science 2008: 51310-51317
126. Sembulingam, K. & Sembulingam, P. (2012). Essentials of medical Physiology, sixth edition. New Delhi: Jaypee Brothers p. 49-62
127. Shier, D., Butler, J. & Lewis, R. (2007). Hole's Human Anatomy & Physiology, Eleventh edition. Boston: McGraw Hill p. 557-588
128. Singh, D., Huntwork, M., Shetty, V., Sequeira, G. & Akingbola, O. (2014). Prolong atrialfibrillation precipitated by new-onset seizures and marijuana abuse. Pediatrics 133(2): 443-446
129. Smith, C. G., Besch, N. F., Smith, R. G. & Besch, P. K. (1979). Effect of THC on the hypothalamic-pituitary axis in the ovariectomized rhesus monkey. Fertil Steril 31: 335-339
130. Smith, N. T. (2002). A review of the published literature into Cannabis withdrawal symptoms in human users. Addiction 97(6): 621-632
131. Solowij, N. & Pesa, N. (2010). Cognitive abnormalities and cannabis use. Brazilian Journal of Psychiatry, 32 (1), 531-540 Retrieved from; ro.uow.edu.au/cgi/viewcontent.cgi?article=1461&context=hbspapers
132. Solowij, N. (1995). Do cognitive impairments recover following cessation of Cannabis use? Life Science 56(23-24): 2119-2126
133. Spiegel, D., Loewenstein, R. J., Lewis-Fernandez, R. (2011). Dissociative disorders in DSM-5. Depressed Anxiety 28(12): 2119-2126
134. Szymanski, H. (1981). Prolonged depersonalisation after marijuana use. American Journal of Psychiatry 138: 231-233
135. Tait, R. J., Mackinnon, A & Christensen, H. (2011). Cannabis use and cognitive function: 8-year trajectory in a young adult cohort. Addiction 106(12): 2195-2203
136. Tennant, F. S. & Groesbeck, C. J. (1972). Psychiatric Effects of Hashish. Archives of General Psychiatry, 27(1):133-136 Retrieved from; https://www.researchgate.net/publication/18135537
137. Thomas, G., Kloner, R. A., Rezkalla, S. (2014). Adverse cardiovascular, cerebrovascular and peripheral vascular effects of marijuana inhalation: what cardiologists need to know. American Journal of Cardiology, 113(1): 187-190
138. Tormey, W. P. (2012). Royal College of Pathologists' autopsy guidelines on sudden cardiac death: roles for cannabis, cotinine, NSAIDs and psychology. Journal of Clinical Pathology 65(2): 187-188
139. Turner, J. C. & Mahlberg, P. G. (1982). Separation of acid and neutral cannabinoids in Cannabis sativa L. using HPLC. In: Agurell S, Dewey W. L. & Willete, R. E. (ed), (1984). The cannabinoids: chemical, pharmacologic and therapeutic aspects. Orlando, Fla: Academic Press Inc. p. 79–88
140. Ungerleider, J. T., Andrysiak, T., Fairbanks, L., Ellison, G. W. & Myers, L. W. (1988). Delta-9-THC in the treatment of Spasticity associated with multiple sclerosis. Advances in alcohol and substance abuse, 7: 39-50
141. United Nations Office on Drugs and Crime (UNODC). World Drug Report, 2008. Retrieved from: www.unodc.org/documents/wdr/WDR2008/WDR2008_cannabis_market.pdf
142. Varsha, Z., Manisha, W., Dinesh, D., Sagar, D., & Uddhao, P. (2013). Antifertility efficacy of *Cannabis sativa* leaves on female albino rats. IJSIT 2(2): 107 – 117
143. World Health Organisation – W.H.O, (1997). Cannabis: a health perspective and research agenda. *Programme on Substance Abuse*, 1997:1(1). WHO REF. No: WHO/MSA/PSA/97.4. Retrieved from: https://iris.who.int/bitstream/handle/10665/63691/WHO_MSA_PSA_97.4.pdf?sequence=1
144. Wikispace, (2013). Free encyclopedia on the effect of Cannabis sativa on the digestive system
145. Witter, K. L. & Niebyl, J. R. (1990). Marijuana use in pregnancy and pregnancy outcome. American Journal of Perinatology, 7(1): 36-38
146. Wright, K. L. (2008). Cannabiniod CB2 receptors in the gastrointestinal tract: a regulatory system in

ISSN No. 2321-2705 | DOI: 10.51244/IJRSI |Volume XII Issue II February 2025

states of inflammation. British Journal of Pharmacology, 152(2): 263-270

147. Zafar, F., Arshad, R., Azeemi, Z. H. & Shaikh, H. A. (1986). A comparative study on the osmotic fragility of erythrocytes in Reptile, Bird and Mammal. Karachi University Journal of Science, 18(1 & 2): 107-117. Retrieved from: https://www.researchgate.net/...comparative_study_on_the_osmotic_fragility _of_eryt...
148. Zambeza (2016). Difference between Cannabis Sativa, Indica and Ruderalis. Retrieved from: https://www.zambeza.com/blog-difference-between-cannabis-sativa-indica-and-rudera.
149. Zavřelová, L. (2017). Cannabis extractions: The complete Guide. Retrieved from: https://medium.com/meetharmony/cannabis-extractions-the-complete-guide-151edb382d65
150. Zerrin, A. (2012). Cannabis, a complex plant: different compounds and different effects on individuals. Journal of Therapeutic Advances in Psychopharmacology, 2(6): 241–254. doi: 10.1177/2045125312457586 Retrieved from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3736954/
151. Zuardi, A. W., Crippa, J. A., Hallak, J. E., Bhattacharyya, S., Atakan, Z., Martín-Santos, R., McGuire, P. K. & Guimarães, F. S. (2012). A critical review of the antipsychotic effects of cannabidiol: 30 years of a translational investigation. Current Pharmaceutical Design; 18(32): 5131-5140 Retrieved from; https://pdfs.semanticscholar.org/aa65/393b024cf93623c2a36cfd11708c4fb9c604.pdf

ISSN No. 2321-2705 | DOI: 10.51244/IJRSI |Volume XII Issue II February 2025

APPENDIX

Tables of Values

RBC Indices

	RBC	Hb	PCV	MCV	MCH	MCHC
Control	5.74	10.5	35.27	61.45	18.29	29.77
	5	11.3	36	72	22.6	31.39
	7.37	12.7	41.77	56.68	17.23	30.40
	7.51	13.3	44.1	58.72	17.71	30.16
	5.29	12	36	68.05	22.68	33.33
Mean	**6.182**	**11.96**	**38.63**	**63.38**	**19.7**	**31.01**
SEM	**0.527**	**0.496**	**1.801**	**2.886**	**1.211**	**0.64**
LD	7.15	12.8	41.56	58.13	17.9	30.80
	7.76	13.4	42.89	55.27	17.27	31.24
	7.13	13.4	43.32	60.76	18.79	30.93
	6.86	12	38.57	56.22	17.49	31.11
	7.03	12.7	39.59	56.32	18.07	32.08
Mean	**7.186**	**12.86**	**41.19**	**57.34**	**17.9**	**31.23**
SEM	**0.152**	**0.26**	**0.922**	**0.971**	**0.264**	**0.22**
HD	7.64	12	39.82	52.12	15.71	30.14
	6.1	10.1	33.86	55.51	16.56	29.83
	7.8	14	45.65	58.53	17.95	30.67
	7.1	12.7	39.97	56.3	17.89	31.77
	6.69	12.3	38.55	57.62	18.39	31.91
Mean	**7.066**	**12.22**	**39.57**	**56.01**	**17.3**	**30.86**
SEM	**0.312**	**0.63**	**1.882**	**1.104**	**0.502**	**0.42**

NaCl Conc. (%)

	0.1	**0.2**	**0.3**	**0.4**	**0.45**	**0.5**	**0.55**	**0.6**	**0.7**	**0.8**	**0.9**	**1**
CONTROL	100	88	58	50	38	0	0	0	0	0	0	0
	100	97	84	84	50	34	0	0	0	0	0	0
	100	80	55	40	15	0	0	0	0	0	0	0
	100	78	76	63	56	34	20	0	0	0	0	0

ISSN No. 2321-2705 | DOI: 10.51244/IJRSI |Volume XII Issue II February 2025

	100	83	75	53	28	0	0	0	0	0	0	0
Mean	**100**	**85.2**	**69.6**	**58**	**37.4**	**13.6**	**4**	**0**	**0**	**0**	**0**	**0**
SEM	**0**	**3.3971**	**5.5911**	**7.46324**	**7.4**	**8.32827**	**4**	**0**	**0**	**0**	**0**	**0**
	100	96	67	42	21	0	0	0	0	0	0	0
LD	100	95	92	82	66	39	29	0	0	0	0	0
	100	95	88	88	64	48	31	12	7	0	0	0
	100	94	86	83	64	31	11	2	0	0	0	0
	100	84	79	79	63	39	24	0	0	0	0	0
Mean	**100**	**92.8**	**82.4**	**74.8**	**55.6**	**31.4**	**19**	**2.8**	**1.4**	**0**	**0**	**0**
SEM	**0**	**2.2226**	**4.3886**	**8.32706**	**8.66372**	**8.29819**	**5.89067**	**2.33238**	**1.4**	**0**	**0**	**0**
	100	89	74	57	38	26	13	0	0	0	0	0
HD	100	92	84	61	37	0	0	0	0	0	0	0
	100	93	86	71	64	52	38	14	0	0	0	0
	100	84	79	69	62	47	31	21	10	0	0	0
	100	92	92	77	69	58	35	12	0	0	0	0
Mean	**100**	**90**	**83**	**67**	**54**	**36.6**	**23.4**	**9.4**	**2**	**0**	**0**	**0**
SEM	**0**	**1.6432**	**3.0659**	**3.57771**	**6.83374**	**10.6189**	**7.28423**	**4.11825**	**2**	**0**	**0**	**0**

ISSN No. 2321-2705 | DOI: 10.51244/IJRSI |Volume XII Issue II February 2025

Table4: Summarised Chart Showing the Effect of High and Low Doses of Cannabis Sativa Leaf Extract on Haematological Parameters of Wistar Rats (N=5)

	Control Group	**Rats Fed With Low Dose (Ld) Of Cannabis Sativa Extract**	**Rats Fed With High Dose (Hd) Of Cannabis Sativa Extract**
Red Blood Cells (Rbcs) Count	6.182 ± 0.527	7.186 ± 0.152	7.066 ± 0.312
Haemoglobin(Hb) Concentration	11.96 ± 0.496	12.86 ± 0.26	12.22 ± 0.63
Packed Cell Volume (Pcv)	38.63 ± 1.801	41.19 ± 0.922	39.57 ± 1.882
Mean Corpuscular Volume (Mcv)	63.38 ± 2.886	57.34 ± 0.971*****	56.01 ± 1.104*****
Mean Corpuscular Haemoglobin (Mch)	19.7 ± 1.211	17.9 ± 0.264	17.3 ± 0.502*****
Mean Corpuscular Haemoglobin Concentration (Mchc)	31.01 ± 0.64	31.23 ± 0.22	30.86 ± 0.42

*Significant: Control group vs. Group fed with Low Dose of Cannabis extract
*Significant: Control group vs. Group fed with High dose of Cannabis extract

Table 5: Summarised chart showing Sodium Chloride (NaCl) Concentrations per Percentage (%) Haemolysis for Osmotic Fragility

	0.1	**0.2**	**0.3**	**0.4**	**0.45**	**0.5**	**0.55**	**0.6**	**0.7**	**0.8**	**0.9**	**1**
Control	100 ± 0	85.2 ± 3.3971	69.6 ± 5.5911	58± 7.4632	37.4± 7.4	13.6± 8.3283	4±4	0±0	0±0	0± 0	0±0	0±0
Low Dose	100±0	92.8± 2.2226	82.4 ± 4.3886	74.8± 8.3271	55.6± 8.6637	31.4± 8.2982	19 *****± 5.8907	2.8 *****± 2.3324	1.4± 1.4	0±0	0±0	0±0
High Dose	100± 0	90 ± 1.6432	83± 3.0659	67± 3.5777	54± 6.8337	36.6± 10.6189	23.4*****± 7.2842	9.4 *****± 4.1183	2±2	0±0	0±0	0±0

*Significant: Control group vs. Group fed with Low Dose of Cannabis extract
*Significant: Control group vs. Group fed with High dose of Cannabis extract