PROJECT COFFEE & HEALTH

Darcy Roberto Andrade Lima

Medical Doctor (M.D.), School of Medicine, Porto Alegre, RGS, Brazil – 1973 Ph.D. on Medicine(Clinical Pharmacology), Royal Hospital of St. Bartholomew, London University,UK – 1982

Post – Doc. ,History of Medicine, London University, UK – 1982

Professor of Medicine and History of Medicine, Neurology Institute, Federal University of Rio de Janeiro, Rio, Brazil (INDC- UFRJ) - present

Associate Director for Medicinal Plants Studies, Institute for Coffee Studies, ICS,

VANDERBILT UNIVERSITY MEDICAL CENTER (VUMC), NASHVILLE, TN,

EUA- present

1. INTRODUCTION

- -At all times and places plants have been domesticated, and the development of agriculture was an intensification by man of his food extractive process. Without the use of cereals man is reduced to an uncertain and unsettled nomadic life.
- -Primitive man, living in a close symbiotic relationship with his environment, was aware of the effects of many plant materials on his mental and physical activities.
- -Simultaneously to the agricultural development, the selection of psychotropic plants has always been one of the most tempting and determined activities of mankind in its history.
- -Nowadays the most consumed plants worldwide are legal ones such as coffee , alcohol (from grapes) and tobacco and illegal ones such as cocaine, opium and cannabis. Why ?

2. WHY ILLICIT CROPS (DRUGS)?

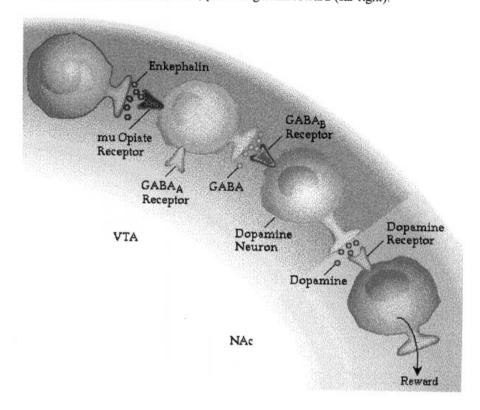
- The plantation, trade, consume and traffic of plants that originates drugs as cocaine, heroine, marijuana is today one of the most important and certainly the most profitable of all world. And there is also the legal plantation of the drug tobacco.
- The illegal drugs trade runs annual resources around US\$ 500,000,000,000.00 (FIVE HUNDRED BILLIONS OF DOLLARS). The American market, the biggest of all world for drugs, created a business that produces annual interests about US\$ 100,000,000,000.00 (ONE HUNDRED BILLIONS OF DOLLARS) twofold more than what the United States spends with petroleum

3. BRAIN REWARD CIRCUITRY

- The brain chemical that leads to depression and compulsive use of drugs with the lost of control, creating the dependence, had begun to be comprehended just recently.
- All drugs of abuse such as the legal ones (nicotine, alcohol) as well as the illegal ones (cocaine, amphetamines, opiates) are typically taken because they produce feelings of euphoria or relieve distress, depression or anxiety. The way drugs cause pleasure or reward, is that they mimic the actions of the neurotransmitters that activate the brain reward circuit
 - The Mesolymbic System VTA >> Nac

Figure 1. Mesoaccumbens Brain Reward Circutry

The mesoaccumbens brain reward circuitry. The three neurons on the left are contained within the ventral tegmental area (VTA) of the midbrain, and the neuron on the right is contained within the nucleus accumbens (NAc). The far left neuron releases the endogenous opiate enkephalin. Enkephalin binds to the mu opiate receptor, which inhibits the g-aminobutyric acid (GABA)-releasing inhibitory interneuron (center, left). The inhibitory interneuron, in turn, holds the dopamine neuron (center, right) in check. Release of GABA stimulates the release of dopamine into the NAc, producing brain reward (far right).



4. WORLD'S MAJOR PROBLEMS

- The prevalence of depression is as high as 20 % among adults into USA and this is a n increasing problem among youth. More than 15 percent commit suicide.
- For white males between 15 and 19 years of age, suicide ranks second among all causes of death.
- 50% of Americans present temporary physical and mental health problems from alcohol ingestion, being that 15% of population is alcoholic. This consumption is increasing among youth in a worldwide basis.
- DEPRESSION: Annual loss of 43.7 billions dollars, accounting work absence, productive reduction, salary expenses, medical treatment and expenses with suicides
- ALCOHOLISM: based on crimes, accidents, productivity changes and health problems, annual loss about 160 billions of dollars in the United States
- Epidemiological studies suggest a n inverse relationship between daily coffee intake and suicide and cirrhosis
- Coffee intake among youth is a controversial and yet unsettled issue

5. WHY COFFEE?

- KING DAVID (1000 to 962 B. C.) " They knew that David and his men would get hungry, thirsty and tired...they brought wheat, barley, meal, *roasted grain*, beans, peas, honey, cheese, cream and some sheep". (2 SAMUEL 17: 28-29) Hebrew's beverage?
- MUHAMMAD (570 632 A . D .) Prophet of Alah "quawa –kaweh coffee"....strength Islamic's beverage?
- Pope CLEMENT VIII (1592–1605) coffee X alcohol: Christian's beverage?

6. COFFEE IS NOT ONLY CAFFEINE

Almost every scientific article published about coffee up to the present focus on its caffeine content and purified cafffeine effects upon the human organism or animal studies. Caffeine is considered the principal psychoactive ingredient of coffee, which may not be true.

Caffeine is one of the most thoroughly investigated ingredient in the human food supply and it is well established that there is no shortage of research on the effects of caffeine on human health.

There are convincing evidences demonstrating that caffeine is safe when consumed in moderation, up to 500 mg daily. Significant health risks may begin to emerge at 500 to 600 mg daily

7. COFFEE IS A MAJOR NUTRACEUTICAL PLANT

Table 1. Substances found into coffee beans and roasted *
Compound Roasting stability Coffee arabica

| CAFFEINE | thermostable | 1 – 1,5 % | 2,0-3,5 |
|-------------------|-------------------------|-----------|-----------|
| % | | | |
| TRIGONELLINE | depends on roasting | 1 % | 0, 75 % |
| NIACIN (Vitamin P | P)depends on roasting | 0,5 % | 0, 5 % |
| CHLOROGENIC AC | CIDSdepends on roasting | 5 – 7 % | 7 – 9 % |
| AMINOACIDS | depends on roasting | 2,0 % | 2,5 % |
| MINERALS SALTS | depends on roasting | 3 – 4,0 % | 4 – 5 % |
| SUGARS | depends on roasting | 50 – 55 % | 35 – 45 % |
| LIPIDS | depends on roasting | 10 - 20 % | 10 – 15 % |
| OTHERS | depends on roasting | 20 - 30 % | 25 – 45 % |

(cafestol, oils, pigments, ashes, water, etc...)

Ref. LIMA, D.R. et al. ACTA PHARMACOLOGICA SINICA, 21 (12), 1057 - 1216), 2000

8. CHLOROGENIC ACIDS FROM COFFEE

.....around 99 % of the people who drink coffee think that coffee is only caffeine....

.....leading american universities and worldwide well recognized research centers are detecting healthy effects of moderate daily intake of coffee (up to 4 cups daily)

.... there is a n inverse relationship between coffee intake and depression/suicide. Depressive illness reaches during any 1 year period almost 18 millions American adults and a significant number of youth. Nearly 11 million americans fail to recognize their illness and get treatment. For white males between 15 and 19 years of age, suicide ranks second among all causes of death; for physicians younger than 40, it ranks first. there is a n inverse relationship between coffee intake and alcoholism/cirrhosis. Around 90 percent of adult people in the world drink alcoholic beverages regularly, and 40 to 50 percent of them, particularly men, have temporary alcohol-induced problems. Around 10 percent of men and 5 percent of women develop persistent alcoholism. In the United States, two- thirds of all adults use alcohol occasionally, and at least 15 percent of the users can be considered "heavy" drinkers. Alcohol dependence is a problem that affects more than 18 millions of Americans and they represent the biggest problem of public health in the United States.

...coronary atherosclerotic heart disease (CAHD) is the commonest cause of cardiovascular disability and death into the U.S.A. Epidemiological studies have identified a number of important risk factors for premature heart disease. These include a positive family history, age, male gender, blood lipid abnormalities, hypertension, physical inactivity, cigarette smoking, diabettes mellitus and hypoestrogenemia in women. Recent case-controlled studies have suggested that depression may be a risk factor for ischaemic heart disease in men but not women and that it is independent of smoking status, diabetes or hypertension. A recent Scottish Heart Health Study has found that increasing coffee consumption was associated with beneficial effects for mortality and coronary morbidity. THE COFFEE HEART STUDY under the author's scientific coordination and Dr. Mario Maranhão,

^{*} coffee to much roasted (very dark roasting) can have mainly caffeine, ashes and traces of the many other compounds

President of the WORLD HEART FEDERATION will be set up on a worldwide basis to test the heart benefits of coffee

....recent studies have detected that coffee has several metabolic effects that could reduce the risk of gallstone formation in men. Cholelithiasis and inflammatory biliary tract disease constitute a major health problem in the USA. Approximately 10% of adults older than 40 years have gallstones and over 10% of men and 20% of women have gallstones by age 65; the total exceeds 20 million people. Although gallstones are more common in women than in men, it increases in incidence in both sexes and at all races with aging. Obesity is a risk factor for gallstones, especially in women, and rapid weight loss, particularly in obese persons increases the risk of symptomatic gallstone formation. In the USA in 1991, more than \$5 billion was expended for the treatment of gallstone disease, and approximately 600,000 cholecystectomies were performed..

.....there is a strong association between coffeee intake and lower incidence of collon cancer. Colorectal cancer is the second leading cause of death due to malignancy in the USA. Approximately 5 % of Americans will develop colorectal cancer with a n estimated 135.000 new cases and 55.000 deaths occurring annualy

.....and coffee is not only caffeine

.....coffee has more than 1.000 compounds such as vitamin PP(niacin) , aminoacids , sugars, lipids, minerals, cafestol, chlorogenic acids (CGA), among many others yet to be studied

... opioid antagonists (naltrexone) are the only FDA aproved medicines to treat alcoholism , a major worldwide problem

...depressed mood is associated with nicotine dependence. Because there is evidence that nicotine activates release of endogenous opioids, the opioid antagonist naloxone has been evaluated in short-term clinical studies for its effect on nicotine abstinence and preliminary data shows that naloxone causes a small but significant decrease in craving and smoking. Recently the FDA has approved the use of na antidepressant, bupropion, as a n adjunct to the treatment of nicotine addiction.

....coffee has far more chlorogenic acids (CGA) with powerfull opioid antagonist activity (6-9~%) than caffeine (1-2,5~%) and when you drink coffee, the CGA goes faster than caffeine into the blood and into the brain. In this way the good mood, lack of depression and of craving for alcohol seems to be related to the CGA from coffee acting into the limbic system while the improvement in attention and memory due to its caffeine content (1-2 %) acting into the brainstem and cerebral cortex. This explains why coffee is not only healthy but the real think drink. And why millions of people enjoy drinking coffee on a daily basis.

...ongoing studies with youth at schools in Brazil are showing that higher rates of participation in school breakfast programs with coffee and milk are associated in a short-term and long-term with improved student functioning on a broad range of psychosocial and academic measures....

.... motor vehicle-related injuries which are the leading cause of death from person aged 1-24 years in the United States being 40 % of these traffic fatalities alcohol-related.....

.... the possibility of coffee intake decreasing or replacing that of alcohol by all drivers must at least be evaluated scientifically as this can save not only thousands of lives but millions of dollars to insurance companies and health care plans....

.... recent data from meta-analysis of research on the behavioral and cognitive effects of xanthines such as caffeine in children have found, "intriguingly that caffeine have a

small, beneficial effect on some children's behaviour, decreasing behaviour that is externalizing or characterized as active, overt, problemating or agressive.....

.... definitively coffee beans , coffee roasting and coffee drinking has yet a lot to be studied under rigorously controlled situations either into laboratories as well as among normal consumers , youth and adults as well as depressed people, alcoholics, smokers and drug addicts, among many others !

...provide the value and the consumption of coffee increases worldwide, all these health problems can have an important decrease for the benefit of mankind

COFFEE KEY REFERENCES AND NEW EVIDENCES:

1. COFFEE PREVENTS SUICIDE:

KLATSKY, A.L. et al. Coffee, Tea and Mortality. ANN. EPIDEMIOL., 1993 (3): 375 - 381.

KAWACHI,I. et.al. A prospective study of coffee drinking and suicide in women. ARCH. INTERN. MED., 1996, 11 (156): 521 - 525

2. CAFFEINE/ COFFEE IS BENEFIC FOR PROBLEMATIC, AGGRESSIVE AND ACTIVE CHILDREN:

STEIN,M.A.,KRASOWSKI,M.,LEVENTHAL,B.,PHILLIPS,W.,BENDER,B.C. : Behavioral and Cognitive effects of methylxanthines : A Meta-Analysis of theophylline and caffeine. ARCH. PEDIATR. ADOLESC. MED., 1996 : 150 : 284 - 288.

LIMA, D.R. I.Q., COFFEE SLEEP AND MEMORY . ECN - EDITORA CIENTÍFICA NACIONAL, RJ, 1995 . 120 p.

MURPHY, J.M., PAGANO,M.E., NACHMANT, J., SPERLING,P., KANE, S., KLEINMAN, R.E. The relationship of school breakfast to psychosocial and academic functioning. ARCH. PEDIATR. ADOLESC. ,MED., 1998: 152: 899-907.

LIMA, D.R. I.Q., COFFEE SLEEP AND MEMORY . ECN - EDITORA CIENTÍFICA NACIONAL, RJ, 1995 . 120 p.

4. OPIOID ANTAGONISTS ARE THE ONLY FDA APPROVED MEDICINES FOR TREATMENT OF ALCOHOLISM:

O'MALLEY, S.S. Opioid antagonists in the treatment of alcohol dependence: clinical efficacy and prevention of relapse. ALCOHOL & ALCOHOLISM, 1996, 31 (1): 77-81

O'BRIEN, C.P. (Chair) . Endogenous opioids in the treatment of alcohol dependence - Meeting report . ALCOHOL, 1996, 13(1):1-39.

5. COFFEE HAS POWERFUL OPIOID ANTAGONISTS:

BOUBLIK,J.H.,QUINNN,M.J., CLEMENTS,J.A., HERINGTON,A.C., WYNNE,K.N. & FUNDER,J.W.: Coffee contains potent opiate receptor binding activity. NATURE, 1983, 301: 246-248

WYNNE, K.N., & FAMILARI, M., BOUBLIK, J.H., DRUMMENT, O.H., RAR, I.D. and FUNDER, J.W. Isolation of opiate receptor ligands in coffee. CLIN. EXPERIMENT. PHARMACOL. & PHYSIOL., 1987, 14: 785-790.

<u>6. COFFEE ACTS ON PREVENTION OF DEPRESSION, ALCOHOLISM AND DRUG</u> DEPENDENCE:

SANTOS, R.M, VIEIRA, S., LIMA,D.R. Effects of coffee in alcoholics. ANN. INT. MED., 1991, 115 (6): 499.

LIMA,D.R.,ANDRADE,G.N.,SANTOS,R.M.&DAVID,C.N. Cigarettes & Caffeine. CHEST, 1989, 95(1): 255-256.

LIMA, D.R. et al. How to give up smoking by drinking coffee. CHEST, 1990,97(1): 254.

SANTOS, R.M. & LIMA, D.R. Coffee as a medicinal plant and vitamin source for smokers. ITALIAN JOURNAL OF CHEST DISEASES, 1989,43(1):56-58.

SANTOS, R.M., OLIVEIRA, D. & LIMA, D.R. . Smoking, Drug Addiction, Opioid Peptides & Coffee Intake. YONAGO ACTA MEDICA, 1990., JAPAN, 33(1): 79-82.

LIMA,D.R. Is coffee good for drug addiction? May Be. AFRICAN COFFEE, JAN 1990, 46-48.

LIMA, D.R. - CAFFEINE AND HEALTH. RECORD PUB., RIO, RJ, 130 P., 1989.

LIMA, D.R. - COFFEE, A MEDICINAL PLANT. VANTAGE PRESS, N.Y., 1990. 120 p.

LIMA, D.R. –I.Q., COFFEE SLEEP AND MEMORY . ECN - EDITORA CIENTÍFICA NACIONAL, RJ, 1995 . 120 p.

FLORES, G., ANDRADE,, F. & LIMA D.R.: Can coffee help fighting the drug problem: preliminary results of the Brazilian Youth Drug Study (BYDS). ACTA PHARMACOLOGICA SINICA, Shangai, 2000, 21 (12): 1059 - 1070.

7. COFFEE'S OPIOID ANTAGONISTS ARE CHLOROGENIC ACIDS:

TRUGO, L.HIGH PERFORMANCE LIQUID CHROMATOGRAPHY IN COFFEE ANALYSIS. Ph.D. THESIS, 1984. UNIVERSITY OF READING, ENGLAND.

TRUGO, L., MACRAE, R. & Dick, J. Chlorogenic acid composition of instant coffee. ANALYST, March 1984, 109: 263-266.

TRUGO, L.C., De MARIA C.A.B., MOREIRA, F.R.A. & PETRACCO, M. Simultanous determination of total chlorogenic acid, trigonelline and caffeine in green coffee by high-performance gel filtration chromatography. FOOD CHEM, 1995, 52:447-49.

8. COFFEE HAS PROTECTIVE EFFECT ON COLON CANCER RISK

TAVANI,A., PREGNOLATO, A., LA VECCHIA C., NEGRI, E., TALAMINI, R FRANCESCHI, S. Coffee and tea intake and risk of cancers of colon and rectum. A study of 3.530 cases and 7.057 controls. INTERNATIONAL JOURNAL OF CANCER, 1997, 73, 193-196.

GIOVANUCCI, E. Meta-analysis of Coffee Consumption of Colorectal Cancer . AM. J. EPIDEMIOL., 1998; 147: 1043-52.

9. DEPRESSION AS A RISK FACTOR FOR CARDIOVASCULAR DISEASES

HIPPISLEY-COX, J., FIELDING, K., PRINGLE, M. Depression as a risk factor for ischaemic heart disease in men: population based-control study. BRITISH MEDICAL JOURNAL, 1998; 316: 1714-1719

10. <u>CAFFEINE IS SAFE ON DOSES UP TO 500 MG DAILY</u>

CURATOLO, P. & ROBERTSON, D. The health Consequences of caffeine. ANN. INTERN.MED, 1983, 98: 641-653.

GRIFFITHS, R.: Human Coffee drinking: manipulation of concentration and caffeine dosage. JOURN. EXP. ANAL. OF BEHAVIOUR, 1986, 45: 133-148,

AMERICAN ASSOCIATION OF FAMILY PHYSICIANS FOUNDATION, USA (INTERNET: http://www.vhs.com/caffeine.html)

INTERNATIONAL FOOD INFORMATION COUNCIL, USA, em CAFFEINE AND HEALTH: clarifying controversies, 3/93, Washington, DC, USA.

LIMA, D.R. CAFFEINE AND HEALTH, RECORD PUB., RIO, RJ, 1989.

JAMES, J.E. - CAFFEINE AND HEALTH, Academic Press, GB, 1991 DEBRY, G. - COFFEE AND HEALTH, JOHN LIBBEY EUROTEXT, Paris, 1994.