

THE EFFECT OF COFFEE CONSUMPTION ON LIVER ENZYMES  
AND BILIRUBIN IN HEALTHY SUBJECTS

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**ABSTRACT:** This study was carried out to determine the effect of coffee consumption on liver enzymes and bilirubin in healthy subjects. Analysis of serum AST, ALT and ALP levels with those of serum bilirubin were carried out. Random blood samples (prior to and after coffee consumption for 2 months) were collected from 58 healthy subjects and the serum liver enzymes (ALP, AST and ALT) and Bilirubin (Total and conjugated) values estimated. Decreased levels of liver enzymes (ALP) and bilirubin are associated with prolonged consumption of filtered coffee by 26 subjects. The initial mean serum values are thus: ALP: 54.08 + 10.63 W/L, AST : 14.04 + 2.75 W/L, ALT: 13: 00 + 2.15 will, Total bilirubin : 0. 54 + 0.17 mg/dl and conjugated bilirubin: +0.28 + 0.08 mg/dl, while the final values are as follows: ALP : 32.04+ 10.69 will, AST : 13.77+2.75 will, ALT: 12.77+ 2.12 W/L, Total bilirubin : 0.07+0.05 mg/dl and conjugated bilirubin 0.07 + 0.05 mg/dl. Also, in 32 subjects placed on unfiltered coffee, elevated levels of ALT and decreased levels of ALP and bilirubin are associated with unfiltered coffee intake. The initial serum liver enzymes and bilirubin levels include: ALP \_ 52.91 + 10.82 iu/L, AST \_ 12.75 + 2.03 iu/L, ALT \_ 13.00 + 2.31 iu/L, Total bilirubin 0.63 + 0.16 and conjugated bilirubin\_ 0.31 + 0.08 mg/dl when compared with the final values\_ of 30.22 + 10.01 for ALP, 14.75 + 2.03 for AST, 29.84 + 2.16 for ALT, 0.12 + 0.05 - Total bilirubin and 0.03 + 0.05 mg/dl for conjugated bilirubin respectively. These observations suggest that prolonged intake of filtered coffee decreases serum concentrations of ALP and bilirubin and has negligible effect on AST and ALT while unfiltered coffee also decreases ALP and bilirubin levels but raises ALT and has no effect on AST levels.

**KEYWORDS:** Liver enzymes, Bilirubin, Coffee, Caffeine.

INTRODUCTION

Coffee beans are the seeds of coffee trees that are widely cultivated in the tropics and these beans have to be roasted and ground before the infusion is made. About 100mg of caffeine and 200mg of tannin in a cup of coffee made by infusing 60g of coffee in a pint (450ml) of water. Analyses of cups of coffee showed that today's Londoners may get from 58 to 168mg of caffeine in a cup of coffee and 43 to 92mg in a cup of tea. Coffee made at home was slightly weaker than that served in cafés (averages 92 and 99mg/cup, respectively), but homemade tea was stronger ([Passmore and Eastwood, 1998](#)). Coffee rapidly loses some of its flavor after grinding; the best coffee is made from beans ground in the home. Preparations of dried ground coffee are convenient but lack bouquet. Instant coffee beans are spray-dried and the powder sold in airtight containers in the home, it is conveniently made into a drink by simply adding warm water. Instant coffees have overtaken traditional ground beans in popularity in many industrial countries. They contain 20 to 40mg of

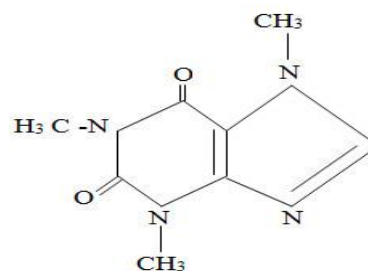
caffeine per gram of powder ([Passmore and Eastwood, 1998](#)).

It is second only to petroleum as a revenue earner; it is an immensely valuable commodity. There is hardly a country in the world that doesn't drink it and around 25million people rely on its production for their livelihoods. Without coffee, many breakfasts and dinner parties would be incomplete and social gatherings the world over would lack an important symbol of hospitality. The Japanese who bathe in coffee grounds believing them to have health giving properties and the Turks, who scan the dregs of their coffee cups for omens of the future, would also have to look elsewhere. The drink that revives hundreds of millions of us (about one-third of the world's population) and especially the Finns who drink an average of five cups each a day, is made from the evergreen shrub now grown in some fifty different countries ([Lewington, 1990](#)). Coffee, being a popular drink in moderate amounts is a mild cerebral stimulant and diuretic. People

habituated to several cups of coffee during the day feel tired if this is stopped and may have headaches. But coffee is not inert. Too much can produce anxiety symptoms, cardiac arrhythmias, Gastrointestinal (GIT) discomfort or insomnia. Some people are more sensitive to the pharmacological actions of coffee or are allergic to it ([Bonati and Garattini, 1988](#); [Passmore and Eastwood, 1998](#)).

The positive aspect of coffee drink is that it offers a pleasant means of increasing fluid intake during a work break or meal. Coffee offers nutrition contributions of potassium and niacin. Any added milk (but not cream) offers protein and sugar as source of energy. Coffee has lower Tannin concentrations which decreases iron absorption and contains caffeine ([Hegarty, 1988](#)). Decaffeinated coffee has most of the taste without most of the pharmacological effects. There is much evidence that caffeine is one of the safest of drugs and reports that it increased the risk of developing coronary heart disease and cancer of the pancreas are not confirmed.

Roasted coffee beans and instant coffee powder contain 10 to 40mg nicotinic acid/100g; the darker the roast the more nicotinic acid. One cup of instant coffee provides around 0.6mg of the vitamin ([Passmore and Eastwood, 1998](#)). Most people are ignorant of the amounts of caffeine they consume and its effects on the body. This is unfortunate, because studies are now linking high caffeine intakes to certain medical problems. The March Dimes recommends that pregnant women limit caffeine consumption to 444mg per day; because research with experimental animals produced birth defects with high caffeine consumption. A long term study has also shown that the risk of coronary heart disease is 2 to 3 times higher in men who are heavy coffee drinkers. The National Academy of Sciences Committee on Diet on Nutrition and Cancer found no strong evidence drinking coffee consumption to cancer. However, caffeine intake may be related to a higher number of non-malignant lumps in the breast of women (4 to 5 cups per day) and to cancer of the ovaries and women with predisposition to develop these types of cancers are urged to drink decaffeinated coffee instead. Researcher Linda Massey of Washington State University showed recently that caffeine increases the body's need for calcium ([Hegarty, 1988](#)). It increases sleep latency, reduces total sleeping time and improves various motor skills impaired by fatigue coffee and caffeine have therefore long attracted attention as potential alcohol antagonists ([Nuotto et al., 1982](#); [Benwitz, 1990](#)).



**Figure 1:** Structure of Caffeine (1,3,7-trimethylxanthine).

## MATERIALS AND METHODS

### 2.1. Subjects

The trial lasted from January to March, 1999. It consisted of a 4 week run in period which served to select those who were able to comply with the requirements, and 8 weeks of treatment (time of coffee consumption).

Volunteers were healthy male and female medical laboratory science students who were recruited from Imo State University, Owerri and their ages range from 19 to 30 years. The study protocol was carefully explained to them before they gave informed consent.

Subjects were eligible if they had body mass index <30kg/m<sup>2</sup>, did not use any drugs known to affect serum concentrations of liver enzymes or bilirubin, were not cigarette smokers, were not pregnant, lactating or on a prescribed diet and avoided methylxanthine foods (cola drinks, tea, cocoa and beverages). Candidates with a history of gastro-intestinal, liver or kidney disease were excluded as were those with glucosuria, proteinuria, anaemia or concentrations of liver enzymes (ALT, AST, and ALP) and bilirubin above the upper limits of normal.

Seventy-six subjects entered a run in period, which served to select those who were able to comply with the requirements. All subjects consumed 3 strong cups (6g in 600ml) of filtered coffee a day. Twelve subjects reported that they could not comply, mainly because they thought that the coffee was too strong. The remaining sixty-four subjects were stratified for sex and liver enzymes and bilirubin concentrations (above or below the median) and allocated them to either filtered or unfiltered coffee by tossing a coin.

In the treatment period, subjects consumed 3 to 4 strong cups (6g in 600ml to 8g in 800ml) a day of either filtered or unfiltered coffee. They were asked to maintain their usual diet and life style. All subjects kept daily records of illness and deviations from the protocol. Body weights were measured monthly.

Five subjects withdrew during the treatment period-two had problems complying, two became ill and one had personal reasons.

Another subject was withdrawn after 4 weeks as his liver enzymes and bilirubin concentrations exceeded the predefined limits. He had started taking drugs with potential hepatotoxicity daily during the treatment period and his data were excluded. Fifty-eight subjects (31 males and 27 females) completed the study.

### 2.2. Blood Samples

Venous blood samples of the 58 subjects were collected and the serum samples obtained after clotting of the blood samples and used to estimate the initial values of liver enzymes and bilirubin of the subjects, that is, before placing them on coffee drink. Another blood samples were equally collected after one month of coffee intake (2 hours after the coffee consumption), and the serum used to estimate the values of liver enzymes and bilirubin of the subjects. Blood samples were also collected after two months of consumption of coffee and used to estimate the final values of liver enzymes and bilirubin of the subjects.

### 2.3. Coffee Preparation

Subjects prepared their coffee at home according to instructions given to them before the study. All ground coffee was NESCAFE (by Nestle, cote d'Ivoire).

For filtered coffee, each subject dissolved 6g of coffee (3 sachets of coffee) with 600ml of hot

water. Then it poured into a paper filter (whatman No.1) in a conical holder which was placed on a thermos flask. They consumed this three times a day (2g in 200ml per cup).

For unfiltered coffee, each subject scooped 8g of coffee (4 sachets) into a flask without filtering it and poured 800ml of hot water onto the coffee grounds. Subjects stirred the mixture so that the coffee will properly dissolve and consumed this four times a day. More coffee was used for the unfiltered so as to provide the same amount of caffeine as filtered coffee. They were allowed to add little sugar (2 cubes per 200ml of water) if they considered the drink too strong.

### 2.4. Biochemical Analysis

Serum AST and were assayed by the method of [Reitman and Frankel \(1957\)](#), ALT was determined by the method of [king and king \(1954\)](#). Also serum bilirubin was determined by the method of [Jendrassik and Groff. \(1938\)](#).

### 2.5. Statistical Analysis

The results were expressed as mean + standard deviation. The statistical evaluation of data was performed using students T-test. A value of  $P < 0.05$  was accepted as significant.

## RESULTS

**Table 1:** Serum liver enzymes (ALP, AST, ALT) and bilirubin (Total and conjugated) level in healthy subjects prior to and after daily intake of filtered coffee for a period of two months

LIVER ENZYMES IN IU/L	SAMPLE NO	INITIAL MEANS+SD	FINAL MEANS+SD	LEVEL OF SIGNIFICANCE
ALKALINE PHOSPHATASE (ALP)	26	54.08+ 10.63	32.04+ 10.69	SIGNIFICANT (P<0.05)
ASPARTATE AMINOTRANSFERASE (AST)	26	14.04+ 2.72	13.77+ 2.75	INSIGNIFICANT (P>0.05)
ALANINE AMINOTRANSFERASE (ALT)	26	13.00+ 2.15	12.77+ 2.12	INSIGNIFICANT (P>0.05)
BILIRUBIN in mg/dl Total	26	0.54+ 0.17	0.07+ 0.05	SIGNIFICANT (P<0.05)
Conjugated	26	0.28+ 0.08	0.07+ 0.05	SIGNIFICANT (P<0.05)

**Table 2:** Serum liver enzymes (ALP, AST, ALT) and bilirubin (Total and conjugated) level in healthy subjects prior to and after daily intake of unfiltered coffee for a period of two months

LIVER ENZYMES IN IU/L	SAMPLE NO	INITIAL MEANS+SD	FINAL MEANS+SD	LEVEL OF SIGNIFICANCE
ALKALINE PHOSPHATE (ALP)	32	52.91+ 10.82	30.22+ 10.01	SIGNIFICANT (P<0.05)
ASPARTATE AMINOTRANSFERASE (AST)	32	12.75+ 2.03	14.75+ 2.03	INSIGNIFICANT (P>0.05)
ALANINE AMINOTRANSFERASE (ALT)	32	13.00+ 2.31	29.84+ 2.16	SIGNIFICANT (P<0.05)
BILIRUBIN in mg/dl Total	32	0.63+ 0.16	0.12+ 0.05	SIGNIFICANT (P<0.05)
Conjugated	32	0.31+ 0.08	0.03+ 0.05	SIGNIFICANT (P<0.05)

## DISCUSSION

In this research, it was found that a daily intake of three to four cups of strong unfiltered coffee raises alanine aminotransferase concentration and decreases alkaline phosphatase and bilirubin concentration in the serum for at least two months. The aspartate aminotransferase was insignificantly raised. The study also showed that daily intake of equivalent amount of filtered coffee decreases alkaline phosphate and bilirubin but do not have any effect on alanine

aminotransferase aspartate. This confirms a case study carried out by [Urgert \*et al.\*, \(1996\)](#), which showed that unfiltered coffee causes an increase in alanine aminotransferase and aspartate aminotransferase but decrease in alkaline phosphate and bilirubin while filtered coffee caused a decrease in liver enzyme (ALP) and bilirubin and has negligible effect on serum a aminotransferases. This is consistent with work of [Fried \*et al.\*, \(1992\)](#).

[Urgert \*et al.\*, \(1996\)](#) compared the long term effects of cafetiere coffee (unfiltered coffee and

filtered coffee) in a randomized controlled trial. Cafetiere coffee raised alanine Aminotransferase concentration in healthy people. The diterpenes cafestol and kahweol in unfiltered coffee are responsible for this effect ([Weusten et al., 1994](#)). They do not pass through paper filters, which explains why filtered coffee does not raise alanine Aminotransferase concentration but they do occur in other unfiltered coffee brews ([Ahola et al., 1991](#); [Carrillo and Bennitez, 1994](#)). Cafestol and kahweol seem to affect liver cells; Long term intake of boiled coffee or preparations rich in cafestol and kahweol raise the serum concentration of alanine Aminotransferase ([Urgert et al., 1995](#)). However, lifelong consumers of boiled coffee in Norway did not have higher alanine Aminotransferase concentrations than consumers of filtered coffee ([Weusten et al., 1994](#)). One explanation for this could be that alanine Aminotransferase concentrations return to normal with prolonged intake of cafestol and kahweol. Thus a high intake of strong unfiltered coffee might explain some cases of raised alanine aminotransferase concentrations in apparently healthy people ([Carola et al., 1990](#)). However, should we really expect unfiltered coffee to affect the risk of liver disease in healthy people? Unfiltered coffee only marginally raised the aspartate aminotransferase concentrations which excludes extensive damage to liver cells. Alkaline phosphatase and bilirubin were reduced rather than raised ([Gu et al., 1992](#)).

In Scandinavian countries, which used to leave high intakes of boiled coffee, death rates from liver cirrhosis are low and seem to be unaffected by the change from drinking boiled coffee to drinking filtered coffee over the past decades ([Kalow et al., 1993](#)).

Therefore, clinically relevant damage to liver cells with regular use of unfiltered coffee appears to be unlikely, although we can not yet fully exclude sub-clinical injury to the liver cells. The decrease in alkaline phosphatase and bilirubin confirms a case control study carried out in an Italian town of Castel Franco Veneto where daily coffee consumption in cups per day inversely correlated with serum levels of liver enzymes and slightly with serum bilirubin ([Casiggia et al., 1992](#)). According to [Casiggia et al., \(1993\)](#) the essential ingredient in coffee for these decreases is Caffeine.

#### CONCLUSION

It has been shown from this study that daily consumption of large amounts of unfiltered coffee raises serum concentrations of the alanine aminotransferase and has no effect on aspartate

aminotransferase, but decreases serum concentrations of alkaline phosphates and bilirubin in healthy subjects for at least two months. The effects on liver enzymes may be innocuous but it might be prudent for patients with raised alanine aminotransferase values to drink more than a few cups of unfiltered coffee on a regular basis.

It can also be seen here that daily consumption of large amounts of filtered coffee decreases serum concentrations of alkaline phosphatase and bilirubin while the concentrations of alanine and aspartate aminotransferase are unaffected

#### REFERENCES

- Ahola I, Jauhainem M, Aro A. The hypercholesterolaemic factor in boiled coffee is retained by a paper filter. *J Intern Med* 1991;236:293-297.
- Benwitz NL. *Clinical Pharmacology of Caffeine*. Mosby Year Book Inc. *Annu Rev Med* 1990;41:277-288.
- Bonati M, Garattini S. Pharmacokinetics of caffeine. *ISI Atlas Science* 1988;2:33-39.
- Carola R, Harley JP, Charles R, Naback P. Functions of the liver. In: *Human Anatomy and Physiology*, McGraw-Hill Publishing Company, New York 1990;pp:707-712.
- Carrillo JA, Bennitez J. Caffeine metabolism in a healthy Spanish population. In: *Clinical Therapeutics*, Mosby-York Book Inc 1994; 55 (3):293-299.
- Casiggia E, Cernetti C, Ambrosio GB. Haemodynamic effects of coffee and purified caffeine in normal volunteers; a placebo controlled clinical study. *J Human Hypertension* 1992;(6):95-99.
- Casiggia SP, Ginocelio G, Ambrosio GB. Unexpected effect of coffee consumption on liver. *Eur J Epidemio* 1993;1:293-297.
- Fried RE, Levine DM, Kwiterovich PO, Diamond EL, Wilder LB, Moy TF, Pearson TA. The effect of filtered coffee consumption on plasma lipid level. *JAMA* 1992;267(6):811-5.
- Gu L, Gonzalez FJ, Kalow W, Tang BK. Biotransformation of Caffeine paraxanthine, theobromine and theophylline by cDNA-expressed human CYP1A2 and CYP21. *Pharmacogenetics* 1992;2:73-77.
- Hegarty V. coffee beverage. In: *Decisions in Nutrition*: Mosby Year book Inc 1988;pp:254-255.
- Jendrassik L, Groff P. Estimation of Bilirubin. *Biochem*1938;297:81.
- King EJ, King PR. Estimation of plasma phosphatase by determination of hydrolysed phenol with amino antipyrone. *J Chem Path* 1954;7:322-326.

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- Kalow W, Tang BK. Caffeine metabolism. In: clinical Pharmacology and Therapeutics. Mosby-year book Inc 1993;53(5):503-507.
- Lewington A. Breakfast drinks from plants. In: Plants for People; Natural history museum Crownwell Road London 1990;pp:84-85.
- Nuotto E, Mattila MJ, Seppala T, Konno K. Caffeine metabolism. In: Clinical Pharmacology and Therapeutics. Mosby-year book Inc 1982;31(1):68-75.
- Passmore R, Eastwood MA. Coffee. In: Human Nutrition and Dietetics. 8th edition, Mosby College Publication 1998;pp:315-317.
- Reitman S, Frankel S. Transaminases. American journal of clinical pathology 1957;28:56.
- Urgert R, Schulz AGM, Katan MB. Effects of Cafestol and Kahweol From coffee grounds and serum lipids and serum liver enzymes in humans. *AM J Clin Nutr* 1995;61:149-154.
- Urgert R, Meyboom S, Kuilman M, Rexwinkel H, Vissers MN, Klert M. Comparison of the Effect of cafetiere and filtered coffee on Serum concentrations of liver Aminotransferases. *British Medical Journal* 1996;313:1396-1412.
- Weusten V, Katan MB, Viani R. Identification of the Cholesterol- Raising Factor from Boiled Coffee and its effect on liver function Enzymes. *J Lipid Res* 1994;35:143-56.