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Caffeine-the Physical Dependence

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ABSTRACT

Caffiene is a xanthine alkaloid which is chemically 1,3,7-trimethyl purine therefore its give cns stimulant activity. caffiene are now-days used in pharmaceutical and beverages(some of the example of beverages' like spike shooter ,wired X344,pepsi,coca-cola,red bull etc) and also some of the pharmaceutical (example are vicks action 500 tab that contain caffeine).but there are safe dose of caffeine is 250 mg/per day. more than 250 mg/per day that may cause some of the side effects like restlessness, irritability, Insomnia, nausea ,but some of the positive effects of caffeine may include diuretic, memory booster, heart protective, liver protective, skeletal muscle relaxant and last found its continue consumption of caffeine may give addiction condition and further some of the withdrawal symptoms found that are anxiety, restlessness, muscle stiffness.

INTRODUCTION

Caffeine is a one of the natural substance that have a activity to central nervous system stimulant. which is chemically 1,3,7-trimethyl purine-2,6-dione.now a more consuming bevarages and cold drink containing caffeine as a active constituents which may act as mood stabilizer and stress free. the safe dose of caffeine is 200 mg in a day may safe but addiction dose may be great than 200 mg per day. therefore addiction of caffeine chances may be great .there are many illegal psychoactive substances like tobacco, opium, but caffeine are legal to consume or sell. there are some of the bevarages contain high amount of caffeine that may addicted to human being like spike shooter, cocaine energy drink etc. now a days in pharmaceutical uses caffeine are preferred, the role of caffeine is analgesic

Futher literature review caffeine consumption in the adults are found in many European countries like Denmark, Switzerland or fi-

Figure 1: Coffee seed.

Product	Serving size	Caffeine content (mg)
Analgesics	2 tablets	64 or 130 mg
Stimulants	1 tablets	100 or 200 mg
Weight-loss products	2-3 tablets	80-200 mg
Sports nutrition	2 tablets	200 mg
Coffee, brewed	8 ounces	135 mg
General foods international coffee, orange cappuccino	8 ounces	102 mg
Coffee, instant	8 ounces	95 mg
General foods international coffee, café Vienna.	8 ounces	90 mg
Maxwell house cappuccino, mocha	8 ounces	60-65 mg
Maxwell house cappuccino, French vanilla or irish cream	8 ounces	55 mg
Maxwell house cappuccino, decaffeinated.	8 ounces	3-6 mg
Coffee, decaffeinated	8 ounces	5 mg
Lipton tea	8 ounces	35-40 mg
Lipton iced tea, assorted varieties	16 ounce bottle	100 mg
Lipton soothing moments blackberry	Tea 8 ounces	25 mg
Tea, green	8 ounces	30 mg
Coca- cola	12 ounces	45 mg
Pepsi- cola	12 ounces	37 mg
Mountain dew	12 ounces	55 mg
Diet coke	12 ounces	47 mg
Sunkist orange soda	12 ounces	40 mg
Barqs diet root beer	12 ounces	0 mg
Juiced	10 ounces	60 mg

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Red-bull	-	80 mg
Monster	-	160 mg
Rock-star	-	160 mg
Full throttle	-	144 mg
No fear	-	174 mg
Amp	-	75 mg
Tab energy	-	41 mg
Wired X505	-	505 mg
Fix	-	500 mg
Bookoo energy	-	360 mg
Wired X344	-	344 mg
SPIKE shooter	-	300 mg
Viso energy vigor	-	300 mg
Cocaine energy drink	-	280 mg
Jolt coca	-	280 mg
sNOS	-	250 mg
Redline RTD	-	250 mg
Blow (energy drink mix)	-	240 mg

aland but also united states or Canada. the most choice bevarge in U.K are tea, soft drink most consumed by united states and percentages is 20% and it is less than mexico or chille. high consumption of caffeine in brazil and argentina due to coffee and yerbamate tea, in china high consumption of green tea[32].

Mechanism of action(3)-

(a)release of ca2+from sarcoplasmic reticulum, especially in sk eletal and cardiac muscle.

(b)inhibition of phosphodiesterase which degrades cyclic nucleotides intracellularly. Then the concentration of cyclic nucleotides is increased. blockade of adenosine acts as a local mediator in the cvs,cns and smooth muscles contracts, especially bronchial dialates cerebral blood vessels, depresses cardiac pacemaker and inhibits gastric secretion, methylxanthines produce opposite effects.

Action(a)is exerted only at concentration much higher than therapeutic plasma concentrations of caffeine (ranging from 5-20μg/ml).then action(b) and(c) are exerted at concentration in the therapeutic range and appear to contribute to bronchodilation, raised cAmp levels in inflammatory cells may attenuate mediator release and promote eosinophils apoptosis adding to the therapeutic effect of theophylline in asthma, adenosine A1 receptor antagonism is considered responsible for cardiac arrhythmias and seizures occurring in theophylline toxicity.

Pharmacological actions(3)-

1)kidney-methylxanthines are mild diuretics; it act by inhibiting tubular reabsorption of na+ and water as well as increased kidney blood flow.

2)smooth muscles-all smooth muscles are relaxed, most prominent effect is exerted on bronchi, especially in asthmatics, then slow and sustained dose-related bronchodilation is produced, but the effect is much less marked compared to inhaled β2 agonists. but vital capacity is increased ,biliary spasm is relieved and effect on intestines and urinary tract is negilible.

3)stomach-methylxanthines enhance secretion of acid and pepsin in stomach,even on parenteral injection and also gastric irritation.

4)skeletal mucles-caffiene enhances contraticle power of skeletal muscles,at high concentration,it increases releases of ca2+from sarcoplasmic reticulum by direct action.but at low doses twitch response to nerve stimulation is augmented,while at toxic doses contracture is produced.

In addition,caffeine facilates neuromuscular transmission by increasing Ach release and its central action relieves fatigue and increases muscular work,enhanced diaphragmatic contractility with theophylline in the therapeutic concentation range probably contributes to its beneficial effects in dysponea and copd

5)CNS- methylxanthines directly cns stimulant. primarly affect the higher centres. caffiene 150250 mg produces a sense of well-being, alertness, beats boredom, allays fatigue,thinking becomes clearer and even when dullness has tended to prevail after a sustained intellectual effort.it tends to improve performance and increase motor active than theophylline in [producing these effects. higher doses cause nervousness, restlessness ,panic, imsomnia and exicement..still higher doses produces tremors, delirium and convulsions. theophylline has greater propensity to produce these adverse effects at higher doses and is definitely more toxic than caffeine.they also stimulate medullary vagal,respiratory and vasomotor centres. vomiitting at high doses is due to gastric irritation and CTZ stimulation.

6)CVS- methylxanthines directly stimulate the heart and increase force of myocardial contractions. they tend to increase heart rate by direct action, but decrease it by causing vagal stimulation ,net effect is variable, tachycardia is more common with theophylline,but caffeine generally decreases heart rate.cardiac output and cardiac work are increased.at high doses cardiac arrythimas may be produced.

While consumption of>9 cups of coffee per day has been found to be assocaiated with increased incidence of methylxanthines, moderate ingestion of caffeine(upto 500 m g/day)does not increase frequency or severity of cardiac arrhythimas ,even in the patients with ischaemic heart diseaeses or preexisting ventricular extrasystoles.

Methylxanthines, especially theophylline dilate systemic blood vessels ,including coronaries by direct actions, peripheral vessels is reduced. however, cranial vessels are constricted especially by caffeine; this is one of the basis of its use in migrane.

7)theophylline decreases release of histamines and other mediator from mast cells and activated inflammatory cells.this may contribute to its therapeutic effects in bronchial asthma.

Pharmacokinetics of caffeine-

1)absorption-

Absorption or bioavailability of caffeine are comparable with all species like human, dogs, rats and mice ,but in animals and humans caffeine is rapidly and completely absorbed in the GIT. then in human beings caffeine is 99% are absorbed within 45 minutes. therefore the plasma concentration of caffeine may decreases rapidly as compare to the paraxanthine. the pharmacokinetics of caffeine is after taking into respiratory system and IV administration are quite similar.then it is absorption more in the acidic environment.

2)distribution-

Caffeine are lipid-soluble compound and therefore it enters blood brain-barrier and placental barrier. then its enter tissue-water compartment and is evenly distributed in all blood plasma ,as including some of the factor like saliva, semen, breast milk and bile. it mechanisms by passive diffusion in a cell layer.

3)metabolism-

Caffeine is metabolized by the two reaction, one is oxidation at C8 position and another is demethylation ,and the involving of the is demethylation. then the involving of the enzyme cytochrome P450 and CYP1A2.therefore some factors that affect caffeine metabolismage,sex,diet,lifestyle,smoking,pregnancy,environmental factors, diseases.

Pharmacodynamics of caffeine(4)-

It acts as an adenosine A2A receptor (ADORAZA).which have ability to perform a stimulating and reinforcing properties of caffeine..

Genetics[4]-

Caffeine dependence study on the heredity of human as comparing to the monozygotic and dizygotic twin and it depends upon polymorphisms in the A2A receptor gene

Positive of caffeine(1)-

* it improves respiratory flow in body and less chances of respiratory disorders.

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* it have less chances of urinary stone(renal stone) in kidney.
* it improve liver functioning.
* it protect against dopamine-acetylcholine in-balance disease.
* it give energy to the muscles
* it may stimulate hair follicles
* it may be increase memory power of brain.
* it may effective in diabetes mellitus type2.
* heart beat may be decreased upto 22% and reduce the blood volume therefore cardiovascular system may be safe
* chances of carcinogen may be reduced.
* it stimulates the central nervous system and make it alert for task or work
* Negative effect of caffeine(1)-
* restlessness.
* insomnia
* bradycardia
* several headaches
* nausea
* heart burn

Withdrawal symptoms(1) *dysphoric mood.

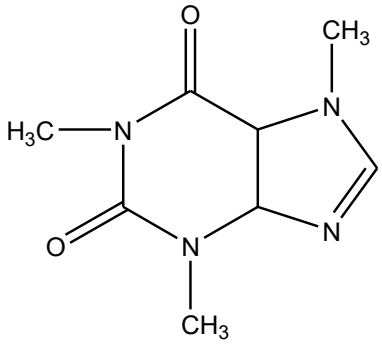
*drowsiness.

*depression.

*fatigue.

structural activity relationship(SAR)-

3,5,7-trimethyl- xanthine is the pharmacophore show the CNS stimulant activity.



Additional mechanism of caffiene

Caffeine act as antagonism of adenosine receptors and also it release purine hormone that present on A1 and A2 receptors that may increase or decrease activity of cyclic AMP ,at the receptor affinity are different for A1 and A2 because one is high and another is low. location of adenosine receptor are brain, cardiovascular, respiratory, renal and gastrointestinal but also in adipose tissue. adenosine receptor non selectively block by caffeine, concentration of caffeine depends upon intake of caffeine containing products. another concept about adenosine that presynaptically it inhibits ach, GABA, dopamine, adrenaline and also serotonin or increasing catecholamine's concentration and reverse the inhibitory effect to the adenosine.(31)

Caffeine-physical dependence

Caffeine that may produce high degree of withdrawal or tolerance that may found regular consumption of caffeine and further some of the symptoms are founding that impaired psychomotor performance, anxiety or it's a common symptoms .plasma concentration of caffeine is found that 12-24 hr at intial and 20-48 hr after of caffeine consumption, withdrawal symptoms may occur first cup of day and after research high caffeine show withdrawal symptoms and another term that highly coffee consumer prefer caffeinated coffee or not decaffeinated coffee(31).

Caffeine addiction or not-

Many doctors tells that high coffee consuming is harmful to health but they do not reponse to it, that condition they found they will addicted, there are three parameter for addiction-psycho activity, drug-reinforced behavior or compulsive use, caffeine may psychoactive therefore coffee consuming is high, that telling reinforced to consumption and depend upon dose or producing dysphoria but addiction of caffeine is not cleared but physical dependence.(31)

Conclusion

Caffeine are xanthine alkaloids therefore consumption of more than 250 mg/per day may be toxic and consumer became addict with caffeine and further some of the extra dose of caffeine give following symptoms like insomnia, heartburn or some of the withdrawal symptoms like anxiety, restlessness or muscle stiffness. pregnant woman and small child must be administration of caffeine with special care. caffeine administration will be clearly monitored and limited

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