Effect of Caffeine on Obesity and Its Application in the Treatment of Obesity

Xinlu Yun
Institute of food, Shenyang Agricultural University, Shenyang, Liaoning, China

Keywords: Caffeine, Obesity, Ephedrine, EGCG, Appetite.

Abstract: Obesity is a chronic metabolic disease, it is not only listed in the top ten chronic diseases by WHO, but also is a risk factor in many other chronic diseases. At present, the treatment of obesity mainly includes lifestyle intervention, drug therapy and surgery. Drug therapy was initially popular as a way to lose weight quickly and has little trauma, but people gradually lost faith in it due to its endless negative news. Therefore it is important to seek a natural substance with very low side effects as a source of drugs for obesity treatment. Caffeine is a natural substance that is ubiquitous found in people's lives, making it more acceptable as a treatment for obesity. Therefore, this paper aims to study the influence of caffeine on obesity, the application of caffeine in the treatment of obesity and the prospect of caffeine as a weight loss drug, expecting to provide new ideas for the development of natural weight loss drugs. Finally, through literature analysis and case studies, it is concluded that caffeine can play a positive role in the treatment of obesity by suppressing appetite and accelerating lipid metabolism, and that the combined use of caffeine with EGCG or ephedrine has a more significant effect than caffeine alone.

1 INTRODUCTION

Due to the development and progress of the Times, a large number of delicious foods, especially the mixture of sugar and oil, appear in people's life. Meanwhile, due to the progress of science and technology, people have less opportunity to put their physical strength into some sports or activities, resulting in the increase of obesity. Obesity is a chronic metabolic disease, it will not only take a toll on health, such as increasing the rate of cardiovascular disease, type 2 diabetes, osteoarthritis and other diseases, but also it will has a great impact on life, and even produce the psychological problems such as depression. Thus, the prevention and treatment of obesity has become today's global hot spots (Seidell 2015). At present, the main treatment methods of obesity include lifestyle intervention, drug therapy and surgery. Among them, most of the studies are related to drug therapy, such as lillutide, which can suppress appetite, orlistat and inhibit lipase activity in gastrointestinal tract. However, there are also many drugs that have been phased out due to the side effects. Therefore, weight-loss drugs with "natural ingredients and low side effects" have also become the focus of research in recent years. Coffeeand tea have always been considered by many people to have the effect of weight loss, but most of the relevant studies on caffeine are about its main ingredient or about its effects on apnea or neurodevelopment treatment of premature infants, and there are few relevant studies in whether it has an impact on obesity treatment and the mechanism of obesity. Thus, this paper will discuss how obesity is produced, whether caffeine has an effect on obesity, the specific application of caffeine in the treatment of obesity and whether it can be widely used as a drug in the treatment of obesity, expecting to provide a safe and effective new idea for obesity treatment and bring help to the obese people.

2 CAFFEINE AND OBESITY

In recent years, refreshing drinks such as coffee and tea have become popular among young people and those who need to stay up late at work. Caffeine has also entered the public's field of vision. However, Chinese and foreign scholars have different views on whether caffeine has an effect on weight loss. On the one hand, some people think that caffeine can suppress appetite and improve metabolism so as to

Yun, X.
Effect of Caffeine on Obesity and Its Application in the Treatment of Obesity.
DOI: 10.5220/0011372000003438
In *Proceedings of the 1st International Conference on Health Big Data and Intelligent Healthcare (ICHIH 2022)*, pages 450-455
ISBN: 978-989-758-596-8

play a role in weight loss, for example, Liu Hanyang (LIU 2016) and Litong Liu (Liu 2018) believe that caffeine can boost lipid metabolism or suppress appetite. On the other hand, some people think that the effect of caffeine on weight loss is not obvious,for example, in the study of Schubert (Schubert 2014) et al, the effects of coffee intake (caffeinated and decaffeinated) on appetite perception and energy intake were investigated and no significant differences were found between the two groups. So in this section whether caffeine could alleviate obesity will be discussed.

2.1 The Emergence of Obesity

Obesity refers to overweight and obesity caused by the accumulation of excessive fat in the body. The pathogenesis of obesity is also very complex. In addition to physiological factors, there are also genetic and environmental factors, but the main causes of obesity are excessive energy intake and metabolic disorders.

Among those factors, energy intake is related to food intake, and food intake is closely related to appetite. Hunger signals due to insufficient energy intake and proximity to delicious food can stimulate appetite and promote eating behavior. And when the body ingests too much, it will also cause the disorder of ingestion control mechanism. For example, the hypothalamus which regulates appetite and energy balance is composed of multiple nuclei: arcuate nucleus (ARC), paraventricular nucleus (PVN), lateral hypothalamic area (LHA), ventromedial nucleus (VMN)and dorsomedial nucleus (DMN). The arcuate nucleus (ARC) located in the central uplift of the hypothalamus, it is considered to be the main region for sensing peripheral metabolic signals. In ARC, two distinct but interrelated groups of neurons are included, one stimulates appetite, including agouti-related (AgR) released by agouti-related peptide (AgRP)neurons and neuropeptide Y (NPY), and the other one suppresses appetite, including proopiomelanocortin (POMC) and cocaine and amphetamine regulated transcript (CART). In addition, some appetite regulation factors such as appetite stimulating ghrelin and appetite suppressing leptin, are also produced by the nucleus of hypothalamus (Zhu 2013).

However, when energy intake is too high, AgRP level can be increassed by reducing POMC and α -melanocyte hormone (α-MSH) expression, thus causing disturbance of feeding control mechanism and energy imbalance, resulting in increased appetite and further fat deposition (Zhu 2013).

Obesity is mostly caused by adipose tissue, it is associated with energy metabolism, brown adipose tissue (BAT) is used to produce heat and white adiposetissue (WAT) is used to store fat, obese patients have more WAT and less BAT but because of the less amount of BAT group, leading to heat production, which regulates metabolism, to break down, causing excess energy to be converted to fat (Liu 2003), It is also one of the causes of obesity.

However, from the perspective of genetics, obesity can also be the result of a combination of genetic and environmental factors. Obesity caused by heredity is divided into single-gene obesity and multi-gene obesity. The pathogenesis of single-gene obesity is mostly caused by abnormal LEP-melanocortin signaling pathway, which is manifested as hyperfeeding and early onset of obesity. While polygenic obesity is generally caused by DNA variation produced by multiple genes, which are significantly associated with BMI,waist circumference, hip circumference and weight (Yu 2020).

To sum up, the causes of obesity are diverse and are not the results of the action of any single factor, so obesity treatment should also be "appropriate to the case".

2.2 Influence of Caffeine on Obesity

Caffeine is a natural methyl xanthine, its chemical name is 1, 3, 7-trimethylxanthine. Caffeine can be found in many plants, such as coffee beans and tea. Caffeine can stimulate the central nervous system, usually dispel fatigue and refresh the brain, and is often used in clinical treatment of neurasthenia and coma resuscitation (Zhang 2021). So it is a popular central nervous stimulant and widely used in food, medicine and other fields. In addition, caffeine also has a certain effect on obesity.

2.2.1 Caffeine's Effect on Lipid Metabolism.

Caffeine can inhibit phosphodiesterase activity and increase cyclic amp depends on protein kinase, and it can induced the downstream of the sympathetic nervous system and hormone sensitive lipase reconciliation coupling protein increases, eventually leading to the increase of energy consumption and fat oxidation (LIU 2016). Because of caffeine's positive impact on the role of fat oxidation, it can enhance the BAT heat production performance, prevent the accumulation of body fat, and play a positive role in the prevention and treatment of obesity.

2.2.2 Caffeine 's Effect on SNS(sympathetic nervous system)

Caffeine can enhance the excitability of sympathetic nervous system (SNS), and SNS plays an important role in adjusting energy consumption and fat metabolism. Norepinephrine (NE) is an important mediator in determining SNS activity, so substance that can stimulate or prolong the presence of NE can increase energy expenditure and promote lipid metabolism. Caffeine can affect activity by inhibiting phosphodiesterase activity, an enayme that can rapidly degrade adenosine monophosphatidylate (cAMP)in cells and is also a signal of reaction to NE (Yang 2019). Besides, neuropharmacological studies have proved that cateholamine like NE, dopamine (DA) and serotonin(5-HT) neurotransmitter changes can change feeding behavior, affect appetite, so the excitement of SNS will have a negative effect on appetite, thus reducing food intake, and because appetite and obesity were positively related, the reduction of appetite will have a positive impact on obesity treatment (Wu 2000).

But the effect of caffeine on obesity depends on the amount of caffeine used, individual differences (age, sex, pregnancy or not), half-life (since caffeine has a shorter half-life, the loner the time passes, the less significant the effect), and whether it is used in combination with other substances.

3 CAFFEINE IN THE TREATMENT OF OBESITY

While many studies have shown that caffeine does suppress appetite and improve metabolism, some studies have shown that caffeine has no significant effect on energy intake or appetite. So given that, it would be more likely for caffeine to work in combination with other substances.

3.1 Synergistic Application of EGCG and Caffeine

Epigallocatechin gallate (EGCG) is the main component of green tea polyphenols. Like caffeine, EGCG is also known for its anti-obesity effects. It also regulates fat metabolism of obese patients, and can stimulate the body to produce heat to accelerate metabolism and reduce the body's absorption of calories from food.

When EGCG is used alone, the possible mechanism of its effect on obesity is that EGCG affects the excitability of SNS, increases energy consumption, and promotes fat oxidation, which in turn drives other mechanisms including changing appetite, up-regulating enzyme activity of liver lipid metabolism, and reducing nutrient absorption. It can be seen from the above that the activity of SNS depends on NE, and EGCG can inhibit the activity of catechol-o-methyl transferase (COMT), which candegrade NE, thus prolonging the survival time of NE. However, due to the low bioavailability of EGCG (< 1%) and the serious side effects associated with high doses of EGCG alone, EGCG in combination with caffeine is a good choice. The combination of EGCG and caffeine can solve the problem that each of them can not be used alone with large doses, and the worry that toxicity may be produced(because they are from the same substance). In addition, one of the reasons for the limited effectiveness of EGCG is also due to the low bioavailability of it, but effective experiments have shown that EGCG with different proportions of caffeine can improve the bioavailability of EGCG. In the study of Yang Z (Yang 2019), all rats were treated according to the experimental design in Table 1: ND group rats had unchanged diet and were given distilled water intragastrically. The other rats were fed high-fat diet, and then randomly divided into five subgroups: obesity group (OB), fed with distilled water. Low EGCG group (LE), gavage 40mg/kgEGCG. High EGCG group (HE), 160mg/kgEGCG. Caffeine group (CF), 20mg/kg caffeine intragastric administration. Low dose EGCG+caffeine group (LE+CF), 40mg/kgEGCG and 20mg/kg caffeine intragastric administration. All the experiments were conducted in the morning, and the volume of intragastic administration was 2ml for four consecutive weeks, and the results were finally obtained as shown in Figure 1. OB group had significant difference in weight gain over 4 weeks compared with ND group. The weight gain of LE group (57.1±8.9g) and CF group (46.2±7.6g) was significantly slower than OB group (75.2±10.6g). But in the HE group (20.3±7.3g) and the LE+CF group (25.4±6.3g),the weight gain retardation effect was more obvious, even lower than the ND group (28.6±4.5g). Therefore, the HE group and LE+CF group achieved the purpose of weight loss, and the effect was better than the LE group and CF group. However, due to the harm of high dose EGCG, it is not suitable for the treatment of obesity, so the combination of caffeine and low dose EGCG can be a good choice for the treatment of obesity.

Table.1: Experimental design and process Quote.

Group name	Group name full name	Feed	Treatment dose
ND	Normal diet group	Ordinary feed	Distilled water
OB	Obesity model group	High fat feed	Distilled water
LE	Low EGCG group	High fat feed	40mg/kg EGCG
HE	High EGCG group	High fat feed	160mg/kg EGCG
CF	Caffeine group	High fat feed	20mg/kg Caffeine
LE+CF	Low EGCG+Caffeine group	High fat feed	40mg/kg EGCG+20mg/kg Caffeine

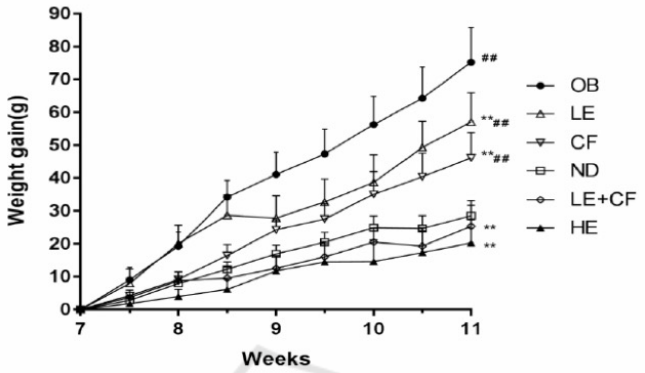

Figure1: Weight trend of rats

About how to mix EGCG with caffeine to get the best results, Litong Liu (Liu 2018) etal discussed the effects of the combined use of EGCG and caffeine on anorexia and fat accumulation in mic in their study, and 15 different concentrations of EGCG and caffeine were used for 8-week experimental study in mice, and the optimal ratio and mechanism of EGCG and caffeine were finally determined. The inhibitory effect of 0.1%EGCG+0.1% caffeine on food intake was the strongest, and the decrease of fat accumulation and body weight was the largest.

In these studies, it was found that the combination of caffeine and EGCG had a more significant effect on obesity and was more helpful in inhibiting weight gain and fat accumulation than using caffeine alone.

3.2 Synergistic Application of Ephedrine and Caffeine

Because caffeine stimulates the sympathetic nerve and thus plays a role in weight loss, it was wondered whether the combination of ephedrine, which also has a central stimulant effect, would make the inhibition of obesity even more significant. Ephedrine is a kind of epinephrine-like drug, and its therapeutic effect is better than epinephrine. It is often used in the treatment of bronchial diseases, etc. For the combined use of ephedrine and caffeine in the treatment of obesity, such auxiliary drugs have been approved to use in foreign countries.

Ephedrine has a similar effect on obesity as EGCG and caffeine, stimulating fat oxidation, increasing energy expenditure and suppressing appetite. Experimental studies indicate that ephedrine can promote the release of catecholamine (CA) transmitters, adrenergic receptors, and promotethermogenesis. However, ephedrine is affected by thenegative feedback regulation of adenosine-prostaglandin and cAMP phosphodiesterase system, they can reduces the thermogenesis effect, but methyl yellow purine compounds can affect the system again, so when the caffeine and methamphetamine collaborative application can enhance the effect of ephedrine, Caffeine also contributes to weight loss by antagonizing adenosine receptors and promoting fat breakdown and thermogenesis (Wu 2000).

In the study of Greenway et al (Greenway 2008), a case study was conducted on 3 patients with hypothalamic obesity who continuously taking caffeine plus ephedrine hydrochloride. The average weight loss of these 3 patients was 13.9%, and two of them maintained weight loss for several years. Although the number of cases is too small to draw definitive conclusions, it is not difficult to see the significant effect of caffeine combined with ephedrine. According to the study of Xiumei Wang et al (Wang 2017), obese rats were divided into control group, caffeine group, ephedrine group and ephedrine combined with caffeine group for a period of 21 days to observe the indexes, and the results in

Table 2 were finally obtained. According to the chart, the weight of the caffeine and ephedrine groups showed little difference from that of the normal control group, but the weight of the ephedrine and caffeine combined group was significantly lower than that of the obesity model group. Therefore, caffeine and ephedrine alone had little effect on weight loss. The combination of ephedrine and caffeine resulted in significant weight loss.

Table 2: Weight data of rats.

Group name	0 weeks weight	1 weeks weight	2 weeks weight	3 weeks weight
Normal Control group	188.23±10.81	251.01±8.55	308.37±20.23	358.03±24.56
Obesity model group	232.22±18.13	330.17±19.23	368.38±7.18	402.70±13.65
Caffeine group	224.42±12.24	243.09±19.03	301.03±22.51	340.36±20.03
Ephedrine group	228.41±18.13	256.31±17.01	310.37±18.53	351.14±17.18
Ephedrine and Caffeine combined group	231.04±11.38	281.36±15.1	310.21±19.25	325.21±21.96

4 DISCUSSION

A large number of studies have confirmed the positive effects of caffeine consumption in the treatment of obesity, diabetes, etc. But whether long-term consumption of caffeine will cause damage to the body is not clear. And the effect of suppressing appetite produced by caffeine has a positive effect on weight loss, but it may cause depression, anxiety and other psychological conditions. In the next place, caffeine's half-life (about 3-4 hours for a healthy adult) makes its effects so short that it is not clear whether it has a long-term lasting effect on obesity. Apart from that, it remains to be seen whether long-term consumption of large amounts of caffeine builds tolerance and weakens weight loss, and whether it leads to dependence.

5 CONCLUSIONS

From the current research, it can be concluded that caffeine does have a certain effect on appetite and metabolism, and because of these effects, it has a certain effect on obesity, so it can be applied in the treatment of obesity. But caffeine alone did not result in the same weight loss as caffeine combined with EGCG or ephedrine. Thus, caffeine alone as a weight loss drug for the treatment of obesity is not easy to achieve, but the combination of caffeine with EGCG or ephedrine and other substances for the treatment of obesity has great prospects.

In addition, during the research process of this paper, there are too few literature about the" influence of caffeine on appetite", so the mechanism of action is not clear.

Currently, there is no complete system of drugs for obesity treatment, and caffeine as a kind of natural substance appears in people's lives almost every day, it certainly is a good choice of weight loss. But there is still a long way to go for caffeine to be widely used to treat obesity, future research is likely to focus on whether there is dependence, resistance, and how to extend the duration action should be researched as well.

ACKNOWLEDGEMENTS

I would like to thank Mr. Li Nuo and Mr. Wang Xiaoying for their help and guidance in this study. I would also like to thank my school shenyang Agricultural University for the cultivation of me, which has laid a solid foundation for me in the professional field.

REFERENCES

Greenway Frank L, Bray George A.Treatment of hypothalamic obesity with caffeine and ephedrine.(2008),Endocrine practice : official journal of the American College of Endocrinology and the American Association of Clinical Endocrinologists, 14 (6) : 697-703.

Litong Liu, Kazutoshi Sayama. (2018)The combined administration of EGCG and caffeine induces not only suppression of fat accumulation but Effects of anorexigenic action on the growth of mice. Journal of Functional Foods,47:156-162.

Liu D, Liu H, Liu H, et al. Lipid metabolism and metabolism of Obesity. (2003)Journal of Clinical Medicine. (03):116-118.

LIU Hanyang, ZHOU Yan, GONG Yu, et al. (2016). J med review, 22(5):928-932. DOI:10.3969/j.issn.1006-2084.2016.05.027.

Schubert Matthew M, Grant Gary, Horner Kat, King Neil, Leveritt Michael, Sabapathy Surendran, Desbrow Ben. (2014)Coffee for morning hunger pangs. An examination of coffee and caffeine on appetite, gastric emptying, And energy intake. Journal of Appetite, 317-26.

Seidell Jacob C, Halberstadt Jutka. (2015)The global burden of obesity and the challenges of prevention.Annals of nutrition & Metabolism, 66 Suppl 2:7-12.

Shurui Yang, Yudian Zhou, Yayuan Wang, Wenyan Wang, Fengxia Liang. (2021) Journal of Huazhong University of Science and Technology (Medical Edition).(04):544-547.

Wang Xiumei, Huang Lichun, Chen Mingying. Effects of combination of ephedrine and caffeine on body weight in rats,(2017)Journal of Pharmacy, (1):29-30.

Wu Ping, Hu Yongshi, Du Qingyun, Chen Hong. Classification and mechanism of weight loss drugs. (2000)Chinese Journal of Clinical Pharmacy, (02):131-134.

Yang Z. The synergistic effect of EGCG and caffeine and the effect of green tea on lipid reduction and weight loss and its mechanism. (2019)Hunan Agricultural University.(01).

Yu Baowen, ZHOU Hongwen. Research progress of genetic obesity. (2020)Journal of Clinical Internal Medicine, (09):611-615.

Zhang Jinyue, Yan Dongying, Gao Liang. Effect of caffeine on central nervous system .(2021)Health Vision, (12):33.

Zhu Yongxiang, Wang Qian, Wang Shuang, Yu Wei, Nan Ying, Cao Jian. (2013)Journal of Jilin University (Medical Edition).(05):1067-1071.