Pathological Mechanisms, Clinical Impacts, Management Strat-egies, and Advances in Innovative Drug Development for Feline Obesity: A Review

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Abstract: Feline obesity, as a prevalent multifactorial nutritional disorder, has seen a significant rise in incidence in recent years, posing serious threats to the health and quality of life of cats. Obesity not only triggers metabolic abnormalities such as insulin resistance and diabetes mellitus but is also closely associated with cardiovascular disease, renal dysfunction, respiratory impairment, and chronic inflammation. Current evidence indicates marked alterations in the gut microbiota composition of obese cats, suggesting a potential role of the microbiota in the pathogenesis of obesity. Furthermore, genetic factors, including variants in the MC4R and POMC genes, are linked to obesity susceptibility. Management strategies for obese cats include dietary modification, exercise intervention, and emerging pharmacotherapies. In recent years, breakthroughs in innovative drug development based on human weight-loss drug experience have been achieved, with GLP-1 receptor agonists, GLP-1/GIP dual-target agonists, SGLT2 inhibitors, and FGF21 agonists showing promising applications. Meanwhile, physical interventions such as peripheral focused ultrasound neuromodulation also offer new ideas for non-pharmacological management. However, challenges including species differences, safety concerns, and clinical trial design still need to be overcome. This review systematically summarizes the epidemiology, pathophysiology, clinical manifestations, diagnostic indicators, management strategies, and advances in innovative drug development for feline obesity, aiming to provide a scientific basis for clinical practice and future research.

Keywords: Feline obesity; metabolic abnormalities; gut microbiota; genetic variation; inflammation; weight management; GLP-1 receptor agonist; FGF21; innovative drugs

1. Introduction

Feline obesity has become a major global challenge in pet health, particularly in the context of rapid

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urbanization. As human lifestyles and dietary habits change, weight management in cats has gained increasing attention. Statistical data show that the prevalence of obesity in cats exceeds 40%, which not only compromises their quality of life but may also lead to a range of serious health problems, including diabetes, joint diseases, and heart disease. According to the 2022 report of the Association for Pet Obesity Prevention (APOP), 61% of cats in the United States are overweight or obese, and over 40% of pet cats in the United Kingdom face the same problem. The number of pet cats in urban China has reached approximately 60 million, with an obesity rate of about 28.1% [1-3]. This high prevalence points to a significant increase in secondary health risks such as diabetes, heart disease, respiratory diseases, and joint problems.

The development of obesity often involves multiple interrelated factors, including genetic predisposition, environmental influences, and inappropriate dietary habits. Among these, lack of sufficient exercise and excessive intake of high-calorie foods are important contributors to obesity in cats. Additionally, as cats age, their basal metabolic rate gradually declines, further increasing the risk of obesity. As obligate carnivores, cats have unique glucose and lipid metabolism profiles, making them more prone to obesity compared to dogs. Studies have shown that for every additional kilogram of body weight, insulin sensitivity decreases by 30%, significantly increasing the risk of type 2 diabetes [4].

Currently, the management of feline obesity primarily relies on non-pharmacological approaches such as dietary control and exercise guidance; however, actual effectiveness is often constrained by multiple factors. Common issues include uncontrolled treat intake, overfeeding by owners in response to begging behavior, and failure to dynamically adjust feeding regimens based on individual metabolic differences. More critically, severe caloric restriction may induce fatal hepatic lipidosis, posing safety risks to non-pharmacological interventions [5]. These difficulties have prompted researchers to explore pharmacological intervention strategies. In recent years, breakthrough advances in human weight-loss drugs, particularly GLP-1 receptor agonists, have provided new research directions for obesity management in companion animals.

To effectively manage and prevent feline obesity, veterinarians and pet owners need to work together to develop scientifically sound dietary plans and exercise regimens. At the same time, individualized management strategies tailored to each cat's lifestyle, health status, and nutritional needs are particularly important. This review delves into the pathological mechanisms of feline obesity, evaluates its impact on feline health, summarizes existing management strategies, and highlights advances and challenges in innovative drug development, aiming to provide valuable references for pet owners and veterinarians.

2. Pathological Mechanisms, Clinical Impacts, and Management Strategies for Feline Obesity

2.1 Epidemiological Characteristics of Feline Obesity

2.1.1 Prevalence and Trends of Obesity by Age Group

Data from large-scale U.S. veterinary hospitals between 2020 and 2023 show a significant upward trend in feline obesity rates. The data indicate that obesity prevalence in adult cats is approximately 15–

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25%, while in senior cats it exceeds 30%. This phenomenon is closely related to pets' lifestyles, dietary habits, and environmental factors. Especially during the COVID-19 pandemic, many cats were confined indoors, leading to reduced energy expenditure and worsening obesity. Moreover, clinical data show that obese cats have significantly higher veterinary visit rates and medical costs, indicating a strong correlation between obesity and health problems [6].

Obesity prevalence in cats varies markedly across age stages. Kittens during growth and development typically have higher nutritional demands and rarely exhibit obesity. However, as age increases—especially into middle and old age—cats' activity levels and metabolic rates decline significantly, raising obesity risk. Studies have shown that obesity in senior cats not only affects their quality of life but may also lead to a range of health issues, including diabetes, arthritis, and cardiovascular disease [7]. Therefore, appropriate management strategies tailored to different age groups are essential for obesity prevention.

2.1.2 Environmental and Behavioral Factors Influencing Obesity

Indoor lifestyle is a major factor contributing to feline obesity. Many cats are confined to the home, lacking sufficient exercise and thereby reducing energy expenditure. Meanwhile, many owners, due to busy schedules, opt for high-calorie, low-nutrition commercial cat foods, further exacerbating the imbalance between energy intake and expenditure. Studies indicate that indoor cats have significantly higher obesity rates than outdoor cats, and the problem worsened during the pandemic when activity time was further reduced [8].

Diet type and feeding practices also significantly influence obesity development. High-fat, high-sugar diets are closely associated with obesity. Many pet owners lack scientific knowledge about feeding, often giving treats or human food indiscriminately, leading to excessive caloric intake. Additionally, the absence of proper dietary plans and exercise schedules makes weight control more difficult. Research shows that comprehensive management strategies involving calorie restriction and increased physical activity can effectively prevent and control feline obesity [9].

2.2 Clinical Manifestations and Impact on Quality of Life in Obese Cats

2.2.1 Potential Impact of Obesity on Feline Quality of Life

Obesity has a significant negative impact on cats' quality of life, mainly reflected in reduced mobility, altered social behavior, and overall health deterioration. Quality-of-life studies indicate that obese cats generally exhibit lower quality of life than normal-weight cats. Pet owners often subjectively perceive reduced activity and health issues in obese cats but may underestimate the overall impact on well-being. According to research, obese cats frequently display reduced movement, lethargy, and social avoidance, which may diminish interactions with owners and other pets, thereby affecting emotional health [10].

Chronic inflammation and metabolic disorders associated with obesity undoubtedly exacerbate health problems, leading to complications such as diabetes, arthritis, and cardiovascular disease, which further impair quality of life. Obese cats often require longer recovery times and more complex treatment plans during veterinary assessments, increasing the financial and psychological burden on owners. Therefore,

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recognizing the potential impact of obesity on quality of life is crucial for veterinarians to provide effective management advice and measures.

2.2.2 Obesity-Related Changes in Respiratory Function

Respiratory function in obese cats is significantly affected, primarily due to mechanical breathing impairments caused by excess weight and metabolic changes. Studies have found that obese cats have lower resting respiratory rates and pulmonary function parameters than normal-weight cats, manifesting as dyspnea and reduced exercise tolerance [11]. Abdominal fat accumulation compresses the diaphragm and thoracic cavity, limiting lung volume and gas exchange efficiency.

Further analysis shows increased airway resistance and decreased lung compliance in obese cats, leading to reduced respiratory efficiency. Dyspnea is particularly pronounced during exercise and may lead to respiratory disorders such as sleep apnea syndrome. Obese cats also face higher respiratory risks during anesthesia and surgery, making them more prone to complications. Thus, veterinarians should integrate weight control with respiratory management when devising treatment plans for obese cats.

2.2.3 Relationship Between Obesity and Renal Function Indicators

Obesity is not only linked to respiratory issues but also closely associated with renal function. Studies indicate that obese cats have significantly elevated renal resistance indices (RI) and abnormal serum SDMA levels (an early marker of renal function), both important indicators for assessing kidney health [12]. Obesity affects renal health through multiple mechanisms, including increased tubular burden, hypertension, and metabolic syndrome-related inflammation.

Obese cats exhibit a clear association with high tubular load and glomerular hyperfiltration, especially when body weight is excessive. Research suggests that obesity may alter glomerular filtration function, thereby reducing the responsiveness to certain drugs and potentially affecting treatment choices and efficacy. Therefore, when managing renal issues in obese cats, veterinarians should prioritize weight management and renal function monitoring to enable early detection of kidney injury.

2.3 Metabolic Abnormalities and Inflammatory Status in Obese Cats

2.3.1 Abnormalities in Blood Pressure and Glucose Metabolism

Obese cats show significant metabolic abnormalities, especially in blood pressure and glucose levels. Studies have demonstrated a close relationship between obesity, hypertension, and hyperglycemia. Obese cats often exhibit metabolic syndrome, including insulin resistance, elevated blood glucose, and dyslipidemia. Specifically, weight gain leads to increased blood pressure, closely related to increased adipose tissue and associated metabolic changes. According to a study on metabolic syndrome, obesity increases cardiovascular risk factors, including hypertension and hyperglycemia, which interact in a vicious cycle [13].

Moreover, the hyperglycemic trend in obese cats should not be overlooked. Obesity-induced insulin resistance causes the pancreas to secrete more insulin to maintain normal blood glucose levels; however,

over time, the pancreas' compensatory capacity declines, potentially leading to diabetes. This hyperglycemic state not only threatens overall health but may also trigger other complications such as cardiovascular and kidney diseases. Therefore, monitoring blood glucose and blood pressure levels in obese cats and intervening promptly is critically important.

2.3.2 Obesity-Related Chronic Low-Grade Inflammation and Oxidative Stress

Obese cats often exhibit a state of chronic low-grade inflammation closely related to obesity-associated metabolic abnormalities. Studies show that obesity not only increases adipose tissue but also triggers a series of inflammatory responses. Specifically, serum amyloid A (SAA) and other inflammatory markers are significantly elevated in obese cats, indicating ongoing inflammation. Additionally, antioxidant capacity is typically reduced in obese cats, making oxidative stress more frequent and further exacerbating inflammation [14].

The mechanisms of chronic low-grade inflammation are closely linked to cytokines, chemokines, and free fatty acids secreted by adipose tissue. These substances not only promote inflammation but may also affect overall metabolic health. Metabolic abnormalities in obese cats may lead to insulin resistance. Research indicates that oxidative stress levels in obese cats are significantly higher than in normal-weight cats, a phenomenon associated with metabolic dysregulation and reduced antioxidant enzyme activity. Therefore, studying and intervening in antioxidant capacity may improve metabolic status and overall health in obese cats.

2.3.3 Obesity and Pancreatic Function/Pancreatitis Risk

Obese cats also exhibit significant pancreatic abnormalities, particularly in the immunoreactivity of pancreatic lipase and trypsin. Studies have found that obesity leads to increased pancreatic fat deposition, which not only affects normal metabolic function but may also increase the risk of pancreatitis. Specifically, the expression levels of lipase and trypsin in pancreatic tissue of obese cats may change, thereby affecting fat and protein digestion and absorption [15].

Furthermore, pancreatic dysfunction in obese cats is characterized by structural changes and aggravated inflammatory responses, potentially leading to pancreatitis. Research shows that obesity induces pancreatic cell steatosis and apoptosis, ultimately affecting overall pancreatic function. Therefore, monitoring pancreatic function and assessing pancreatitis risk are important components of managing the health of obese cats. Targeted dietary interventions and appropriate exercise may help reduce these risks.

2.4 Changes in Gut Microbiota of Obese Cats and Their Significance

The gut microbiota plays a key role in metabolic regulation in obese cats. Research has shown that obese cats exhibit significant alterations in gut microbiota composition, which not only affect energy metabolism but may also be closely related to obesity development. The pathological mechanisms of obesity involve multiple factors, among which changes in the composition and function of the gut microbiota are considered critically important. Studying the gut microbiota of obese cats helps deepen our understanding of the causes of obesity and potential interventions.

2.4.1 Diversity and Compositional Changes of Gut Microbiota in Obese Cats

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Obese cats show markedly reduced diversity and altered composition of gut microbiota. Studies indicate that the ratio of Firmicutes to Bacteroidetes increases significantly in obese cats, with an increase in Firmicutes abundance and a decrease in Bacteroidetes abundance, a change closely related to obesity [16-17]. Increased abundance of specific bacterial groups, such as certain Proteobacteria and Enterobacteriaceae, has also been observed in association with obesity. This microbial dysbiosis not only affects food digestion and energy absorption but may also increase the risk of various metabolic diseases.

Moreover, changes in gut microbiota are closely related to cats' dietary habits. High-fat diets significantly alter gut microbiota composition, further exacerbating the pathological process of obesity. Dietary modifications, such as increasing dietary fiber intake, can improve gut microbiota diversity, thereby counteracting obesity and its related metabolic diseases [18].

2.4.2 Association Between Gut Microbial Function and Energy Metabolism

Gut microbes not only affect intestinal health but also directly participate in regulating energy metabolism. The gut microbiota of obese cats influences fatty acid synthesis pathways through various mechanisms, thereby altering the host's energy metabolism. For example, microbial metabolites such as short-chain fatty acids (SCFAs) play an important role in fat metabolism by stimulating the secretion of gut endocrine hormones that regulate appetite and energy balance [19]. In obese cats, changes in gut microbiota may activate fatty acid synthesis pathways, exacerbating fat accumulation and energy imbalance. Microbes affect the host's energy acquisition and storage patterns through specific metabolites. Therefore, interventions targeting the gut microbiota, such as probiotics or dietary changes, may effectively improve the metabolic status of obese cats.

2.4.3 Impact of Weight Loss on Gut Microbiota

Standardized weight loss programs can significantly alter the abundance and diversity of gut microbiota in obese cats. Research has found that after weight loss intervention, the gut microbiota of cats develops toward a more diverse and healthier state, with an increase in Bacteroidetes abundance and a decrease in the Firmicutes ratio. These changes are closely associated with weight loss and metabolic improvement [17,19]. Further studies indicate that weight loss not only reduces body weight but also enhances intestinal health and overall metabolic function by modulating gut microbiota composition. Dietary intervention and appropriate exercise can effectively promote gut microbiota remodeling, playing an important role in obesity management. Therefore, future management of obese cats should consider gut microbiota modulation as a potential therapeutic strategy.

2.5 Research Progress on Obesity-Related Genes and Molecular Mechanisms

2.5.1 Association Between MC4R Gene Variants and Feline Obesity

The MC4R (melanocortin-4 receptor) gene plays an important role in the genetic study of obesity, particularly in feline obesity. Research has shown a significant association between MC4R gene variants (SNPs) and body mass index (BMI). According to a systematic review, over 200 MC4R variants have been documented, with a frequency of 1% to 6% in obese individuals [20]. Specific SNPs have been found to be closely related to appetite regulation and energy balance, and their functional relevance is strong. Variants

may lead to increased appetite and reduced energy expenditure, thereby promoting obesity. For example, certain loss-of-function MC4R variants are closely associated with higher body weight and fat accumulation in cats. These findings not only provide important evidence for understanding the genetic basis of feline obesity but also offer potential genetic targets for precision therapy.

Further research indicates that abnormal activation of the MC4R signaling pathway is closely linked to obesity-related metabolic diseases such as diabetes and cardiovascular disease. These findings underscore the importance of MC4R in the pathophysiology of obesity and provide new perspectives for developing gene-based interventions.

2.5.2 Novel Variants in the POMC Gene and Their Potential Pro-Obesity Effects

The POMC (pro-opiomelanocortin) gene plays a key role in energy metabolism and body weight regulation. Recent studies have identified significant associations between POMC gene polymorphisms and obesity phenotypes. For instance, certain POMC variants may affect hunger and satiety sensations, leading to increased energy intake and weight gain [21]. Moreover, these variants may interfere with adipose tissue metabolism and inflammatory responses through neuroendocrine pathways, further exacerbating obesity development.

Studies in children and adolescents have found that certain POMC polymorphisms are closely related to BMI changes, suggesting that early identification of these genetic markers may help develop personalized obesity intervention strategies. This indicates that POMC polymorphisms play an important role not only in the pathogenesis of obesity but may also serve as potential therapeutic targets.

2.5.3 Changes in Obesity-Related Gene Expression and Metabolic Impact

In obesity, gene expression in muscle and adipose tissue undergoes significant changes closely related to metabolic disorders. Research shows that in obese individuals, the expression of pro-inflammatory genes in adipose tissue is significantly increased, while that of anti-inflammatory genes is decreased, creating a state of chronic low-grade inflammation [22]. This inflammation not only affects adipocyte function but also interferes with systemic metabolic balance.

In muscle tissue, obesity is associated with decreased expression of metabolism-related genes (such as AMPK, PGC-1α, etc.), which may lead to insulin resistance and reduced fatty acid oxidation capacity. Further studies have found that specific dietary and lifestyle interventions can partially restore normal expression of these genes, thereby improving metabolic status and reducing the risk of obesity-related complications. These findings provide new molecular targets and strategies for obesity management, emphasizing the importance of considering gene expression regulation in obesity treatment.

2.6 Hormonal Changes and Endocrine Effects in Obese Cats

Hormonal changes in obese cats are closely related to endocrine disorders, affecting their overall health. Obesity not only manifests as weight gain but also represents changes in metabolic status. Hormones play important roles in regulating energy balance, metabolism, and appetite, and alterations in hormone levels in obese cats may lead to a series of health problems, including diabetes and liver disease. Therefore, understanding hormonal changes and their endocrine effects is crucial for developing effective

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management strategies.

2.6.1 Molecular Network of Appetite Regulation

The maintenance of food intake and energy balance relies on a complex signaling network, the core of which consists of two functionally antagonistic classes of peptide molecules: orexigenic peptides that promote appetite and anorexigenic peptides that suppress appetite. These molecules establish bidirectional communication between the central nervous system and peripheral organs, collectively maintaining the body's energy homeostasis [1,5].

Orexigenic peptides mainly include ghrelin, phoenixin, and asprosin. Among these, ghrelin, a 28-amino acid peptide hormone, not only stimulates appetite but also participates in the regulation of growth hormone secretion while directly targeting muscle cells to promote muscle protein synthesis, offering unique value in maintaining lean body mass [4]. Anorexigenic peptides are represented by glucagon-like peptide-1 (GLP-1), glucose-dependent insulinotropic polypeptide (GIP), leptin, and nesfatin-1. GLP-1, secreted by intestinal L cells and released after meals, acts by delaying gastric emptying, promoting insulin secretion, and centrally suppressing appetite. GIP belongs to the same incretin family as GLP-1, and the two synergize to produce stronger metabolic improvement effects, which forms the theoretical basis for dual-target strategies [4].

2.6.2 Association of IGF-1 Levels with Obesity and Obesity-Related Diseases

Insulin-like growth factor-1 (IGF-1) is a polypeptide hormone synthesized by the liver and closely related to growth hormone. Studies have shown that IGF-1 levels are typically significantly elevated in obese cats, which is closely associated with increased body fat and metabolic disturbances. Elevated IGF-1 concentrations in non-diabetic obese cats may be due to the influence of cytokines and hormones secreted by adipose tissue on IGF-1 synthesis and metabolism. Moreover, the endocrine environment of obese cats may further exacerbate this process, and obese cats often exhibit pituitary enlargement, suggesting adaptive changes in the pituitary gland due to increased metabolic load.

Elevated IGF-1 is closely linked to the development of various obesity-related diseases. For example, IGF-1 may promote adipocyte proliferation and differentiation, exacerbating fat accumulation and thus obesity. IGF-1 is also considered to be associated with the development of diabetes; although elevated IGF-1 in non-diabetic obese cats does not directly cause diabetes, it may play a role in the development of metabolic syndrome. Changes in IGF-1 levels in obese cats are closely related to insulin resistance and hepatic steatosis. Therefore, monitoring IGF-1 levels can provide important biomarkers for the management of obese cats.

2.6.3 Metabolic Regulatory Role of FGF21 Pathway Activation

Fibroblast growth factor 21 (FGF21) is a newly discovered hormone involved in regulating various metabolic processes. FGF21 expression levels are typically elevated in obese cats, and its activation may be closely related to changes in energy metabolism. Research suggests that FGF21 may play a key role in regulating obesity and related metabolic diseases by influencing fatty acid oxidation and insulin sensitivity. Therefore, the study of the FGF21 pathway provides new ideas and potential therapeutic targets for obesity

intervention. In recent years, metabolic regulators have gained increasing attention in feline obesity research. FGF21 plays an important role in energy metabolism, glucose homeostasis, and fatty acid oxidation. In obese cats, FGF21 expression levels typically change, which may be related to increased adipose tissue and altered metabolic load.

The application of FGF21 agonists has shown significant efficacy in studies of obese cats. Experimental results indicate that FGF21 agonists can effectively reduce body weight in obese cats and improve hepatic fat accumulation. FGF21 helps improve the metabolic status of obese cats by promoting fatty acid oxidation and inhibiting fat synthesis. Additionally, FGF21 can reduce insulin resistance by enhancing insulin sensitivity, providing a better metabolic environment for obese cats. In summary, FGF21 plays a key role in metabolic regulation in obese cats. Activating the FGF21 pathway not only helps reduce body weight but also improves endocrine disorders associated with obesity.

2.7 Nutritional Requirements and Dietary Management of Obese Cats

The management of obese cats is a complex process that requires in-depth exploration of their specific nutritional needs and dietary management strategies. Optimizing nutritional requirements not only aids weight loss but also improves overall health. As obesity becomes increasingly prevalent in cats, scientists are focusing on how dietary management can effectively control weight and improve quality of life.

2.7.1 Assessment of Essential Amino Acid and Vitamin Intake During Caloric Restriction

Assessing essential amino acid and vitamin intake in obese cats during caloric restriction is crucial. According to the National Research Council (NRC) recommendations, cats require specific amino acids and vitamins to maintain physiological functions. However, in practice, many cats' diets may not meet these needs, especially during weight loss. Studies have shown that deficiencies in certain essential amino acids (e.g., lysine, methionine) and vitamins (e.g., A and E) may lead to immune dysfunction, skin problems, and other health issues [6]. Therefore, when formulating weight loss plans, ensuring that the diet provides adequate nutrients is essential to avoid potential health risks.

Moreover, research indicates that caloric restriction in obese cats may affect amino acid metabolism, particularly during weight loss. Long-term caloric restriction may lead to loss of muscle mass, thereby affecting metabolic rate and health. Therefore, during weight loss programs, regular monitoring of body weight and nutritional status is recommended to adjust dietary plans promptly, ensuring that cats receive necessary nutrients while losing weight [23].

2.7.2 Application of Low-Carbohydrate, High-Protein Diets

Low-carbohydrate, high-protein diets are increasingly recognized in the management of obese cats. Studies show that this dietary pattern not only aids weight loss but also improves metabolic health. For cats with diabetes and obesity, excessive carbohydrates may cause blood glucose fluctuations, whereas high-protein diets provide a more stable energy source, helping control weight and blood glucose levels [24].

More importantly, low-carbohydrate, high-protein diets can promote fat oxidation, assisting in fat metabolism during weight loss. This dietary pattern may enhance satiety, reducing food demand and making

weight control easier. Additionally, adequate protein intake helps maintain muscle mass, which is especially important for obese cats because preserving muscle tissue during weight loss helps stabilize basal metabolic rate [25].

2.7.3 Adjuvant Effects of Natural Anti-Inflammatory and Antioxidant Compounds

The introduction of natural anti-inflammatory and antioxidant compounds shows positive potential in the management of obese cats. Research indicates that obese cats typically exhibit chronic low-grade inflammation, closely related to obesity-associated metabolic diseases. Incorporating natural anti-inflammatory and antioxidant compounds containing plant extracts and active ingredients can effectively alleviate obesity-induced inflammatory responses, thereby improving health and quality of life [8].

For example, certain plant extracts such as green tea extract and turmeric extract have been found to possess significant antioxidant and anti-inflammatory effects, helping reduce obesity-related inflammation. Furthermore, natural antioxidants can enhance the immune system and improve overall health. Combined with appropriate dietary strategies, the application of these natural compounds may provide additional health benefits for obese cats, aiding in weight management and metabolic function improvement. Therefore, considering the addition of these natural ingredients may be an effective adjunctive strategy when formulating dietary plans for obese cats [26]. Resveratrol, another natural polyphenol, has been shown in studies to improve lipid metabolism disorders in obese cats, but its weight-loss effect as a standalone intervention is limited [4].

2.8 Weight Management Strategies and Clinical Interventions for Obese Cats

2.8.1 Communication Strategies Between Veterinarians and Pet Owners

Effective communication between veterinarians and pet owners is crucial in managing obese cats. Research suggests that veterinarians should emphasize the impact of obesity on cats' life expectancy and prioritize this information in communication. Obesity not only reduces cats' quality of life but may also shorten their lifespan and increase the risk of chronic diseases such as diabetes and arthritis [6]. Therefore, veterinarians can help pet owners recognize the importance of weight management by providing detailed information on obesity-related diseases and preventive measures.

Additionally, veterinarians should employ appropriate communication techniques to help pet owners understand and accept their cats' obesity problems. Using simple language, charts, and examples, veterinarians can effectively convey the potential health hazards of obesity. At the same time, when advocating behavioral changes, veterinarians should respect pet owners' opinions and feelings, encouraging them to participate in the cat's management plan. Research shows that actively engaged owners are more likely to implement long-term dietary and exercise changes, thereby improving their cats' health [24]. Finally, regular follow-up and feedback are important components of communication strategies. Through regular check-ups and weight assessments, veterinarians can adjust management strategies in a timely manner and provide feedback to owners. This ongoing communication and support can enhance pet owners' confidence in the management plan, increasing their willingness and effectiveness in implementation.

2.8.2 Exercise Intervention and Behavioral Modification

Increasing physical activity is an important strategy for weight control in obese cats. Research shows that appropriate exercise can significantly increase energy expenditure and promote weight loss [25]. To achieve this goal, veterinarians can develop individualized exercise plans based on each cat's needs and lifestyle. Additionally, veterinarians should educate pet owners on how to increase their cats' activity levels in daily life. For example, using interactive toys, setting up obstacles, or engaging in play can effectively stimulate cats' interest in exercise.

Behavioral modification is also an important component of exercise intervention. Many cats are unwilling to exercise due to lack of interest or habitual behaviors, so veterinarians can help owners identify and change these undesirable habits. Taking small steps to gradually acclimate cats to new activity patterns can increase their participation. Additionally, using positive reinforcement (such as treats or praise) to encourage cats to exercise is an effective behavioral modification strategy.

Notably, exercise intervention should be combined with dietary management to ensure cats receive adequate nutritional support. When implementing exercise and behavioral modifications, veterinarians should regularly assess cats' health status to adjust plans as needed, ensuring safety and health [9].

2.8.3 Emerging Pharmacotherapies and Future Perspectives

With a deeper understanding of the pathological mechanisms of feline obesity, emerging pharmacotherapies are continuously being developed. Among novel drugs, GLP-1 receptor agonists, GLP-1/GIP dual-target agonists, SGLT2 inhibitors, and FGF21 agonists show promising application prospects.

(1) GLP-1 Receptor Agonists (Single Target)

GLP-1 receptor agonists are currently the most 关注 category in the field of human weight-loss drugs. Their mechanism of action involves reducing caloric intake through dual pathways—suppressing the appetite center and delaying gastric emptying—while improving insulin sensitivity and reducing the risk of diabetes complications [1]. Applying these drugs to pet obesity treatment has become an important direction for researchers. Currently, studies are underway to evaluate the weight-loss effects of GLP-1 receptor agonists in overweight and obese domestic cats. Preclinical data show that these compounds can safely and effectively limit food intake in experimental animals [4]. GLP-1 receptor agonists help achieve weight loss in cats by suppressing appetite and increasing energy expenditure [27].

(2) GLP-1/GIP Dual-Target Agonists

Dual-target agonists act on both GLP-1 and GIP receptors, aiming to achieve superior metabolic improvement through multi-pathway synergy. The design concept of these drugs originates from successful experiences in human medicine, and they have entered clinical research stages for feline obesity intervention. Available research data indicate that these drugs can achieve safe weight loss within a relatively short dosing period, providing preliminary clinical evidence for the application of dual-target strategies in cats [4].

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(3) SGLT2 Inhibitors

SGLT2 inhibitors, as metabolic regulators, achieve dual effects of glucose lowering and weight loss by inhibiting renal glucose reabsorption and increasing urinary glucose excretion. They have entered clinical trials for feline diabetes and are expected to be extended for the treatment of simple obesity [1]. These drugs promote weight loss by increasing urinary glucose excretion and may improve the metabolic status of cats [28].

(4) FGF21 Agonists

As described in section 2.6.3, FGF21 agonists, as novel metabolic regulators, can help reduce body weight by improving insulin sensitivity and promoting fat oxidation [16]. Clinical research on these drugs is ongoing and shows potential for weight control in cats.

(5) Other Metabolic Regulators and Anti-Inflammatory Drugs

Based on the "inflamm-aging" pathological mechanism of feline obesity, drugs targeting inflammatory pathways and metabolic regulation have become important research directions. Resveratrol, a natural plant polyphenol, has been shown in studies to significantly decrease plasma triglycerides, free fatty acids, and serum amyloid A concentrations while increasing adiponectin concentrations in obese cats after four weeks of continuous supplementation; however, its weight-loss effect as a standalone intervention is limited [4].

Comparison of Characteristics of Different Technological Approaches

Technological Approach	Route of Administration	Characteristics	Challenges
GLP-1/GIP dual-target agonist	Injection	Significant weight-loss effect, preliminary clinical data validation	Requires regular injection, high pet compliance requirements
Long-acting GLP-1 implant	Subcutaneous implantation	Stable dose release, high compliance	Implantation procedure required, higher cost
Oral small-molecule GLP-1 agonist	Oral administration	Convenient administration, high pet acceptance	Bioavailability challenges, difficult R&D
GLP-1 single-target agonist	Injection	Mature technology, good safety profile	Weight-loss effect may be weaker than dual-target
Natural product modulator	Oral	High safety, anti-inflammatory effects	Limited weight-loss effect as

Currently, drug development for feline obesity is active worldwide. GLP-1 receptor agonists and their related derivatives are research hotspots in this field, with researchers in multiple countries conducting drug evaluations at various stages from preclinical to clinical. In terms of formulation innovation, research on long-acting sustained-release formulations is advancing, aiming to reduce dosing frequency and improve medication compliance. The development of oral small-molecule GLP-1 receptor agonists is also being explored, seeking to achieve non-injectable administration routes by improving bioavailability. Current research projects cover multiple stages from laboratory studies to clinical evaluations, with some candidate drugs having entered clinical trial phases. Primary evaluation indicators include changes in body weight, improvements in metabolic parameters, and safety profiles. Most study designs employ randomized controlled protocols to obtain reliable pharmacodynamic and safety data [1-4].

2.8.4 Physical Intervention: Peripheral Focused Ultrasound Neuromodulation (pFUS)

Peripheral focused ultrasound neuromodulation is an emerging non-invasive technique that modulates metabolic function by targeting peripheral sensory nerves. In the field of metabolic regulation, the target of pFUS is primarily the hepatic sensory nerves. One study explored for the first time the safety and potential efficacy of pFUS in cats. Phase 1 verified safety in healthy cats, showing no adverse events. Phase 2, conducted in overweight and obese cats, also showed no adverse events and observed a significant decrease in plasma glucose, with decreasing trends in interstitial glucose and triglycerides [4]. This study confirms the feasibility of pFUS in cats, offering a non-pharmacological option for future feline obesity management.

2.8.5 R&D Challenges and Safety Issues

Species Differences and Pharmacological Safety: Cats have significantly different physiological and metabolic characteristics from humans and dogs, rendering some human weight-loss drugs inapplicable. For example, long-term use of sulfonylurea oral hypoglycemic agents in cats leads to islet amyloid deposition [1]. Some studies have pointed out that GLP-1 receptor agonists may excessively stimulate insulin release while strongly inhibiting gastrointestinal emptying, leading to adverse reactions such as vomiting and anorexia [2]. Historical experience provides a scientific 警示: a weight-loss drug for dogs was previously approved for marketing, which reduced appetite and lipid absorption by inhibiting microsomal triglyceride transfer protein. However, a considerable proportion of treated animals experienced vomiting and diarrhea, and some exhibited anorexia symptoms, ultimately leading to market withdrawal due to safety and tolerability issues [3,4]. Additionally, cats are highly sensitive to caloric restriction, and weight-loss drugs must precisely control the rate of weight loss to ensure a safe range of 0.5-1% weekly weight loss, thereby preventing complications such as hepatic lipidosis [1,5].

Clinical Trial Design and Execution Challenges: Pet drug clinical trials face multiple challenges including sample recruitment, cycle control, and standardization of execution. Clinical trials for feline obesity require strict control of variables such as diet and exercise, demanding high compliance from pet owners

and increasing the complexity of trial execution [2]. Furthermore, according to relevant regulatory requirements, veterinary drugs for clinical trials must undergo inspection by specialized institutions and follow corresponding regulatory guidelines. Study design and implementation processes must meet rigorous scientific standards [3,4].

2.9 Comprehensive Management of Obesity-Related Diseases in Cats

Comprehensive management strategies are particularly important when dealing with obesity-related diseases in cats, including early screening for cardiovascular and renal diseases and the development of integrated treatment plans. Obesity not only affects cats' quality of life but also significantly increases the risk of cardiovascular disease (CVD) and chronic kidney disease (CKD). Studies show that obese cats commonly have hypertension, diabetes, and other metabolic diseases, which in turn exacerbate renal burden and lead to worsening renal function [29-30]. Therefore, early screening is crucial for identifying these potential risks. Regular blood tests and imaging assessments can help detect problems early. At the same time, comprehensive treatment plans for cardiovascular and renal diseases should include dietary control, appropriate exercise, and necessary pharmacological interventions.

2.9.1 Prevention of Obesity-Related Cardiovascular and Renal Diseases

Early screening and comprehensive treatment plans for obese cats are particularly important to promptly identify and address potential health risks. Monitoring obesity should incorporate multiple indicators such as body weight, heart rate, blood pressure, and renal function assessments. Research results indicate that the risk of cardiovascular disease in obese cats is significantly higher than in normal-weight cats, closely related to obesity-induced metabolic disorders [30]. Therefore, regular comprehensive health check-ups are recommended clinically, especially for middle-aged and senior cats, with a full examination every six months to enable early identification of potential cardiovascular and renal risks.

In comprehensive treatment strategies, dietary intervention is foundational. Research indicates that low-calorie, high-fiber diets aid weight loss and improve cardiovascular health. At the same time, appropriate exercise should not be overlooked, as it promotes metabolism and enhances cardiovascular function. Additionally, for hypertension and renal insufficiency caused by obesity, veterinarians may consider using ACE inhibitors to control blood pressure and reduce renal burden [29]. Treatment plans should be individualized and adjusted based on each cat's specific health status and response.

2.9.2 Association Between Obesity and Diabetes Mellitus and Key Management Points

The relationship between obesity and diabetes is primarily manifested through insulin resistance mechanisms. Excessive accumulation of adipose tissue in obese cats, especially visceral fat, often leads to impairment of insulin signaling pathways, resulting in insulin resistance [31]. This resistance reduces the efficiency of glucose utilization, ultimately leading to hyperglycemia and diabetes.

For this mechanism, management strategies should focus on weight loss and improving insulin sensitivity. Research shows that caloric restriction and increased exercise can significantly enhance insulin sensitivity in obese cats. Additionally, the use of specific drugs, such as GLP-1 receptor agonists, has shown potential for improving glycemic control [32]. Comprehensive management plans should include dietary adjustments, exercise programs, and possible pharmacotherapy to achieve better glycemic control and weight

management.

2.9.3 Intervention in Chronic Inflammation and Metabolic Syndrome

Chronic inflammation plays a key role in the metabolic syndrome of obese cats, leading to a series of health problems such as diabetes and cardiovascular disease. Research indicates that adipose tissue in obese cats contains large amounts of inflammatory factors, which not only promote local inflammatory responses but also affect systemic metabolic status [33]. Therefore, anti-inflammatory treatment is an important measure to improve the health of obese cats.

Lifestyle modifications, including diet and exercise, are the foundation of anti-inflammatory treatment. Low-sugar, low-fat, high-fiber diets help reduce systemic inflammation levels. Additionally, increasing daily activity and reducing sedentary time have been shown to effectively alleviate inflammatory responses. Regarding pharmacotherapy, certain anti-inflammatory drugs or supplements, such as fish oil and antioxidants, may help alleviate chronic inflammation in obese cats [31]. The combined application of these measures can help improve the overall health of obese cats and reduce the risk of related diseases.

3. Conclusion

Feline obesity, as a complex multifactorial disease, is increasingly attracting attention in veterinary medicine. Through in-depth research into genetic, metabolic, inflammatory, and microbiota-related mechanisms, we can more comprehensively understand the impact of obesity on cats' quality of life and health. Obesity not only significantly reduces cats' activity levels and quality of life but also predisposes them to various complications such as diabetes, arthritis, and cardiovascular disease. These risks make obesity management an indispensable issue in veterinary practice.

Current research has revealed obesity-related gene variants (such as MC4R, POMC) and changes in the gut microbiota. These findings provide new therapeutic targets and may enable precision medicine. By integrating genomics and microbiome studies, we can better understand the biological basis of obesity and develop more effective interventions. Meanwhile, dietary regulation and exercise intervention remain core strategies for managing obese cats. Effective dietary plans must consider not only energy requirements but also nutrient balance to ensure cats' health during weight loss.

In terms of innovative drug development, GLP-1 receptor agonists and their related derivatives, based on human drug experience, are currently the most 关注的 technological direction, with preliminary research data demonstrating their weight-loss potential. Diverse approaches, including GLP-1/GIP dual-target strategies, FGF21 agonists, SGLT2 inhibitors, long-acting formulations, oral formulations, and non-pharmacological physical interventions (such as pFUS), are all being explored. However, challenges including pharmacological safety issues due to species differences, difficulties in clinical trial execution, and lessons learned from historical drug development all indicate that cross-species drug research requires the establishment of independent evaluation systems tailored to feline metabolic characteristics.

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The key to successful weight loss lies in effective communication between veterinarians and pet owners. Veterinarians need to provide scientific guidance and support, helping owners understand the health impact of obesity and develop practical weight loss plans. Pet owners should actively participate, regularly monitor their cats' weight and health status, and provide feedback to veterinarians to adjust management strategies. Only through such collaboration can the success rate of weight loss be improved.

Future research should further explore the molecular mechanisms of feline obesity and the clinical effects of interventions. We should focus on early identification and prevention of obesity to reduce its long-term impact on feline health. Additionally, as research progresses, novel pharmacotherapy strategies are expected to play a more active role in the weight loss process. Future feline obesity management may exhibit the following trends: multi-target combinations (developing from dual-target to triple-target agonists), long-acting formulations, oral administration routes, personalized therapy (combined with biomarker testing), and integrated interventions (combining drugs with prescription diets, weight monitoring, exercise guidance, etc., to form an integrated management model). Through scientific approaches including target optimization, formulation innovation, and combined interventions, feline obesity management is expected to move toward more precise and safer comprehensive treatment strategies.

In summary, the management of feline obesity requires multidisciplinary collaboration, advancing the field through the integration of scientific research and clinical practice. With a deeper understanding of feline obesity, we have reason to believe that the health and quality of life of cats will be significantly improved.

References

[1] Chen Wenqin, et al. Causes and Comprehensive Prevention of Obesity in Dogs and Cats [J]. Breeding and Feed, 2025,24(04):102-105.

[2] Ji Benlei. Causes and Treatment of Obesity in Pet Cats [J]. Animal Husbandry and Veterinary Science and Technology Information, 2024(01):193-196.

[3] Chen Yingni. Causes and Treatment of Obesity in Pet Cats [J]. Veterinary Guide, 2020(09):53.

[4] Ye Yanlin, Bai Zhengguang, Zhang Binkai, et al. Etiological Analysis and Management of Obesity in Dogs and Cats [J]. Shanghai Journal of Animal Husbandry and Veterinary Medicine, 2015(01):62-63.

[5] Liu Kai. Causes and Treatment of Obesity in Pet Cats [J]. Journal of Traditional Chinese Veterinary Medicine, 2018(05):71-72.

[6] Ajoolabady A, Liu S, Klionsky DJ, et al. ER stress in obesity pathogenesis and management. Trends Pharmacol Sci. 2022;43(2):97-109.

[7] Krishnamoorthy M, Nadler E, Vaidya S. Resolution of confluent and reticulated papillomatosis after bariatric surgery. Clin Obes. 2021;11(1):e12427.

[8] Mandal AK, Sahoo A, Almalki WH, et al. Phytoactives for Obesity Management: Integrating Nanomedicine for Its Effective Delivery. Nutr Rev. 2024. Online ahead of print.

Corresponding author：Huang chao，Email:67731020@qq.com

[9] Jung MH, Ihm SH. Obesity-related hypertension and chronic kidney disease: from evaluation to management. Kidney Res Clin Pract. 2023;42(4):431-444.

[10] Oesch-Régeni B, Schultes B. [Obesity and kidney disease]. Ther Umsch. 2024;81(3):83-89.

[11] Lazzaro A, De Girolamo G, Filippi V, et al. The Interplay between Host Defense, Infection, and Clinical Status in Septic Patients: A Narrative Review. Int J Mol Sci. 2022;23(2).

[12] Chen Y, Dabbas W, Gangemi A, et al. Obesity Management and Chronic Kidney Disease. Semin Nephrol. 2021;41(4):392-402.

[13] Richter-Stretton GL, Fenning AS, Vella RK. Skeletal muscle: A bystander or influencer of metabolic syndrome? Diabetes Metab Syndr. 2020;14(5):867-875.

[14] Ansari P, Khan JT, Chowdhury S, et al. Plant-Based Diets and Phytochemicals in the Management of Diabetes Mellitus and Prevention of Its Complications: A Review. Nutrients. 2024;16(21).

[15] Vélez-Bonet E, Gumpper-Fedus K, Cruz-Monserrate Z. Exploring the Role of Hyperinsulinemia in Obesity-Associated Tumor Development. Cancer Res. 2024;84(3):351-352.

[16] Fan S, Chen S, Lin L. Research progress of gut microbiota and obesity caused by high-fat diet. Front Cell Infect Microbiol. 2023;13:1139800.

[17] Sehgal K, Khanna S. Gut microbiota: a target for intervention in obesity. Expert Rev Gastroenterol Hepatol. 2021;15(10):1169-1179.

[18] Puca P, Petito V, Laterza L, et al. Bariatric procedures and microbiota: patient selection and outcome prediction. Ther Adv Gastrointest Endosc. 2021;14:26317745211014746.

[19] Savytska M, Kozyk M, Strubchevska K, et al. Association between intestinal microflora and obesity. Minerva Gastroenterol (Torino). 2024;70(3):342-352.

[20] Fatima MT, Ahmed I, Fakhro KA, Akil ASA. Melanocortin-4 receptor complexity in energy homeostasis, obesity and drug development strategies. Diabetes Obes Metab. 2022;24(4):583-598

[21] Vourdoumpa A, Paltoglou G, Charmandari E. The Genetic Basis of Childhood Obesity: A Systematic Review. Nutrients. 2023;15(6).

[22] Wu P, Guo L, Li X, et al. Comprehensive analysis of epigenomics and transcriptome data to identify potential target genes associated with obesity. Front Genet. 2022;13:1024300.

[23] Tantisattamo E, Kalantar-Zadeh K, Halleck F, Duettmann W, Naik M, Budde K. Novel approaches to sarcopenic obesity and weight management before and after kidney transplantation. Curr Opin Nephrol Hypertens. 2021;30(1):14-26.

[24] Ghusn W, Loftus EV Jr, Johnson AM. Reviewing the impact of obesity on inflammatory bowel disease and considerations for optimizing management. Curr Opin Gastroenterol. 2024;40(4):268-275.

[25] Khakoo NS, Ioannou S, Khakoo NS, Vedantam S, Pearlman M. Impact of Obesity on Inflammatory Bowel Disease. Curr Gastroenterol Rep. 2022;24(1):26-36.

[26] Johnson AM, Loftus EV. Impact of Obesity on the Management of Inflammatory Bowel Disease. Gastroenterol Hepatol (N Y). 2020;16(7):350-359.

[27] Jadidi S. A Review of Non-Surgical Pain Management in Osteoarthritis. Cureus.

2020;12(10):e10829.

[28] Kalra S, Verma M, Arora S, Kapoor N. The octagon of opportunities in obesity. J Pak Med Assoc. 2024;74(10):1886-1887.

[29] Yang H, Ying J, Zu T, Meng XM, Jin J. Insights into renal damage in hyperuricemia: Focus on renal protection (Review). Mol Med Rep. 2025;31(3).

[30] Dousdampanis P, Aggeletopoulou I, Mouzaki A. The role of M1/M2 macrophage polarization in the pathogenesis of obesity-related kidney disease and related pathologies. Front Immunol. 2024;15:1534823.

[31] Yadav U, Kumar N, Sarvottam K. Role of obesity related inflammation in pathogenesis of peripheral artery disease in patients of type 2 diabetes mellitus. J Diabetes Metab Disord. 2023;22(1):175-188.

[32] Tarazi MS, Touhamy S 2nd, Tchang BG, Shukla AP. Combined medical strategies for the management of type 2 diabetes mellitus and obesity in adults. Expert Opin Pharmacother. 2021;22(16):2199-2220.

[33] Hamjane N, Benyahya F, Nourouti NG, Mechita MB, Barakat A. Cardiovascular diseases and metabolic abnormalities associated with obesity: What is the role of inflammatory responses? A systematic review. Microvasc Res. 2020;131:104023