Diabetes mellitus (DM) is commonly diagnosed in cats. In humans, treatment regimens for non–insulin-dependent DM include various combinations of dietary modification, exercise, insulin administration, and one or more oral antidiabetic drugs, which have been extensively evaluated in humans but not in cats. Glucose toxicity is a phenomenon of chronic hypoglycemia and must be understood before interpreting response to any antidiabetic therapy. This article provides a critical review of the oral antidiabetic drugs glipizide, metformin, troglitazone, and acarbose.

Diabetes mellitus (DM) is a common endocrine disorder in cats. It is estimated to affect 1 in 300 cats, with both forms of the disease defined by the ability of pancreatic beta cells to secrete insulin. Type I DM is characterized by the destruction of insulin-producing beta cells in the islets of Langerhans. Type I DM is always insulin dependent; therefore, the treatment of choice is insulin. Type II DM is characterized by defects in glucose-stimulated insulin secretion by the pancreas and in peripheral tissue sensitivity to and use of insulin. Initially, type II DM is non–insulin-dependent because of the ability of beta cells to produce some insulin. However, the progression of disease usually results in insulin dependence.

In humans, treatment options for type II DM include various combinations of dietary modification, exercise, and administration of one or more oral antidiabetic drugs with or without insulin. The treatment options for type II DM in cats are not as diverse as those for humans for the following reasons:

- It is difficult to discern in cats whether DM is insulin dependent, and most cats are treated as insulin-dependent diabetics.
- Diabetic cats with finicky appetites may be difficult to manage with dietary changes.
- Oral antidiabetic drugs have not been extensively evaluated in cats. (Nevertheless, understanding their possible role in treating feline diabetics is important for veterinarians. Use of these drugs in cats may become more commonplace, and clients often have questions regarding their use.)
In general, oral antidiabetic drugs act by stimulating insulin secretion, decreasing hepatic gluconeogenesis, or improving muscle and adipose tissue sensitivity to insulin. Because type II DM is a progressive disease that ultimately requires insulin injections and/or multiple drug therapies, careful patient selection is essential for these drugs to be used successfully.

Due to the high incidence of diabetes, diabetic complications, problems with long-term insulin use, and the hospital time and resources spent on managing diabetes in humans, diabetologists have studied alternatives to insulin over the past 30 years. Similar investigations are needed in cats in light of the high euthanasia rate of diabetic cats (30% to 40%) and the knowledge gained in humans on the effects of diet, exercise, and antihyperglycemic drugs on glycemic control.

The following factors are used to evaluate the efficacy of antidiabetic drugs:

- The difference between pretreatment and posttreatment fasting blood glucose (FBG) and postprandial blood glucose (PPBG) concentrations
- Similar differences in glycosylated hemoglobin (HbA1c) or serum fructosamine concentrations
- Pretreatment factors serving as positive predictors of response to therapy
- Causes of failure to respond

**SULFONYLUREAS (GLIPIZIDE)**

Sulfonylureas were found to have the potential to treat diabetes over 50 years ago when researchers were studying their antibiotic effects. Sulfonylureas are highly protein-bound derivatives of the sulfa antibiotics. Glipizide is a second-generation sulfonylurea; first-generation drugs of this class have less potency and higher polarity, are less lipid soluble, and have not been examined for use in cats. Sulfonylureas are well absorbed from the gastrointestinal (GI) tract. There are some weakly active or inactive metabolites produced in the liver. The liver and kidney clear sulfonylureas; hepatic inactivation is the primary route of clearance.

The sulfonylureas are the only class of antihyperglycemic drug with a direct mechanism of action at the pancreatic beta cell. The insulinotropic effect of sulfonylureas is depicted in Figure 1.

Other effects of sulfonylureas have also been described. There is in vitro evidence for a decrease in hepatic gluconeogenesis, an increased number of insulin receptors in tissues of action, and increased postinsulin receptor activity.

**Efficacy**

**Humans**

In humans with type II diabetes, glipizide decreases the FBG level by 60 to 70 mg/dl and the HbA1c by 1.5% to 2%, which is similar to the efficacy of insulin. In humans, factors that predict a positive response to sulfonylureas include diabetes diagnosed within the past 5 years, hyperglycemia in the range of 220 to 240 mg/dl, adequate beta-cell function as measured by a high fasting C-peptide level, and no history of exogenous insulin treatment. The likelihood of response to glipizide treatment is inversely correlated with the degree of blood glucose elevation at the start of therapy. Therefore, carefully selecting patients with mildly to moderately elevated fasting and postprandial glucose levels for glipizide therapy is recommended and may improve efficacy.

Failure of humans to respond to therapy as evidenced by an acceptably minimal decrease in glucose concentrations after 3 months of therapy is related to patient factors (noncompliance, coexisting disease), drug factors (use of medications that antagonize insulin action or secretion, inadequate drug dosage), and disease progression. A 6-year follow-up of humans treated with sulfonylureas showed that only 5% (33 of 660) maintained normoglycemia. This attests to the nature of type II DM as a progressive disease and the eventual need for multidrug therapy, including insulin.
**Cats**

The data on efficacy of glipizide in cats is complicated by the uncertainty of the underlying diabetic state (type II versus type I DM) and the absence of blinded, placebo-controlled prospective clinical trials. The first study of glipizide in cats examined its effect on serum insulin and glucose concentrations in 10 healthy cats. Mean serum insulin concentration increased for 1 hour after glipizide administration, and mean serum glucose concentration decreased within 15 minutes of glipizide administration, with the lowest concentration at 60 minutes and duration of effect up to 120 minutes. In a 1993 study of 20 cats, Nelson and colleagues found improved clinical signs and blood glucose concentrations in 65% (13 of 20) of cats with DM that were treated with glipizide. This included five cats that were considered complete responders based on resolution of clinical and laboratory indices of diabetes by the fourth week of therapy. Eight cats considered to be partial responders did have resolution of clinical signs but remained hyperglycemic (greater than 200 mg/dl) and glucosuric.

In 1997, Feldman and coworkers monitored glycemic control in feline diabetics treated with only glipizide for 50 weeks. Glycemic control was achieved in 44% (22 of 50) of cats. These cats were further classified as complete responders (14%), partial responders (12%), transient diabetics (12%), and transient responders (6%). However, three of these cats had long-term treatment failure, reducing the overall success rate to 38%. Results of long-term follow-up in a number of these diabetic cats supported the presence of type II DM and its progressive nature. The relationship between the degree and duration of hyperglycemia prior to therapy and the likelihood of response to glipizide in cats is unknown. Other predictive factors for determining response to therapy in cats are also unknown. Therefore, conservative patient selection promotes a better success rate when using glipizide in cats. Guidelines for patient selection as well as therapeutic protocols have been described.

**Side Effects**

**Humans**

In humans, adverse effects of sulfonylureas are typically mild and reversible upon discontinuation of drug administration. The most important side effect of therapy is hypoglycemia, which is estimated to occur in 2% to 4% of humans treated for type II DM with a sulfonylurea. For comparison, the incidence of hypoglycemia due to insulin therapy is the same. Other common side effects include cutaneous rashes and GI disturbance, while less common side effects include mild thrombocytopenia, mild hemolytic anemia, and high liver enzyme activity.

Risk factors that predispose humans to adverse effects include decreased glomerular filtration rate, hepatic insufficiency, mild DM (mean serum glucose concentration of 140 mg/dl), and the simultaneous use of drugs that interact with the pharmacokinetics of sulfonylureas (e.g., aspirin, trimethoprim, H₂-blockers, warfarin, β-adrenergic blockers, sympatholytic drugs, thiazides, loop diuretics, corticosteroids).

**Cats**

The incidence of side effects due to glipizide in cats was 16% in 50 cats treated for 50 weeks. Commonly reported side effects are high liver enzyme activity, hepatotoxicity, anorexia, and vomiting, all of which may resolve with temporary discontinuation of the drug. Liver enzyme activity may return to normal despite continued administration of glipizide, suggesting that elevated liver enzyme activity may be seen with or without underlying hepatotoxicity. GI side effects resolve or improve by administering the drug with food. Based on current information, the incidence of hypoglycemia (usually asymptomatic) ranges between 12% to 15%. The incidence of mild hypoglycemia may be underestimated due to the subtle clinical signs associated with its occurrence.

**BIGUANIDES (METFORMIN)**

Metformin is a biguanide antihyperglycemic agent. The active component, guanidine, is found naturally in animal and plant material and explains the medieval European practice of administering components of the French lilac flower (Galega officinalis) to diabetic patients. Unlike glipizide, it is not highly protein bound or metabolized. To date, there are two reports of metformin pharmacokinetics in cats. The mean oral bioavailability in six healthy adult cats was found to be 48%. The peak plasma concentration occurs between 1 and 3 hours after oral administration. Ninety percent of the drug is excreted in the urine within 12 hours of administration.

Because metformin improves insulin sensitivity in peripheral tissues, it is not effective in the absence of insulin. Whereas glipizide results in an increase in serum insulin concentration to lower blood glucose, metformin results in a decrease in serum insulin concentration.

In humans and rats, therapeutic concentrations of metformin in the liver result in improved insulin-induced suppression of hepatic gluconeogenesis, which correlates with decreases in FBG concentrations.
Also, glucagon-induced gluconeogenesis is reduced. In myocytes, metformin increases the activity of the insulin receptor tyrosine kinase and enhances the number and activity of the glucose-transporter-4. Uptake of glucose by muscle, muscle glycogen formation, and glucose oxidation are all increased. In adipose tissue, metformin increases the uptake and oxidation of glucose and increases the binding of insulin to its receptors. The antilipolytic action of insulin is thereby reduced, causing weight loss even when diet and exercise are held constant. This benefit in obese patients is in contrast to insulin and glipizide therapy, which increases insulin concentrations. Metformin has no effect on insulin production or secretion at the pancreatic beta cell.

**Efficacy**

**Humans**

When used as monotherapy in humans, the FBG level decreases by a mean of 60 to 70 mg/dl and the Hb A1c concentration by a mean of 3%. When compared with other therapies (insulin, glipizide), metformin causes a greater decrease in the PPBG concentration compared with the FBG concentration.

When used in combination therapy with a sulfonylurea in humans, the FBG decreases by 63 mg/dl more than with sulfonylurea alone. When patients with poorly controlled type II DM on insulin were treated with metformin, Hb A1c concentrations were significantly lower compared with placebo and there was improved glycemic control with the use of 30% less insulin. This indicates that the hypoglycemic effect of metformin is additive to that of sulfonylureas and insulin in humans, a concept that has not been studied in cats.

Primary treatment failure, defined as failure to achieve glycemic control at the onset of therapy, occurs at an overall incidence of 12% in humans. As with most patients, the incidence of secondary treatment failure (failure to maintain target glycemic levels after an initial positive response) with metformin increases with duration of therapy because of the progressive nature of type II DM.

**Cats**

Recently, five newly diagnosed diabetic cats and one acromegalic diabetic cat that was on insulin therapy were given metformin (10 mg sid to 50 mg bid PO). Clinical signs, blood glucose, serum fructosamine, and Hb A1c values did not improve after 7 weeks in three cats. There was no improvement in the cat with diabetes and acromegaly. One cat developed ketoacidosis, and one was found dead (cause unknown) 2 weeks after initiating metformin administration. One cat achieved improved glycemic control for 5 months and then developed acute pancreatitis and loss of glycemic control. There are no other published data on the efficacy of metformin in cats. It has been speculated that many cats suffer from glucose toxicity as a result of chronic hyperglycemia (Box 1); therefore, improving insulin sensitivity in peripheral tissues by using metformin may provide little benefit in cats with glucose toxicity.

**Side Effects**

**Humans**

The overall incidence of adverse effects of metformin treatment in humans is 20% to 30%. The most common effects are diarrhea, nausea, abdominal pain, and a metallic taste. Side effects can be minimized by taking metformin with food and by slowly increasing the dose in small increments once therapy is initiated.

Hypoglycemia is a rare occurrence in humans treated with metformin alone because the drug does not increase insulin secretion. An uncommon yet potentially fatal adverse effect of metformin therapy documented in humans is lactic acidosis, with an estimated incidence of 0.027 to 0.06 cases per 1000 patient-years. Metformin precipitates lactic acidosis by promoting the formation of lactate; the amount of lactate produced is limited by the amount of substrate available (glucose).

**Box 1**

**Chronic Hyperglycemia: A Brief Review**

Chronic hyperglycemia causes pancreatic beta cells to be desensitized to glucose, resulting in impaired insulin secretion. In addition, there is relative insulin resistance in peripheral tissues. Insulin receptors can move beneath the cell membrane as a result of chronic hyperglycemia, and the glucose transport systems become dysfunctional. The end result is a low serum insulin concentration with hyperglycemia (this is in contrast to insulin resistance, characterized by a very high insulin concentration accompanying hyperglycemia). Glucose-induced desensitization of the pancreas and peripheral tissues is reversible. Glucose toxicity is the term used for an irreversible state of beta-cell dysfunction and resembles type I DM because the pancreas becomes unresponsive after stimulation by insulin secretagogues despite its ability to produce insulin. Therefore, results of insulin secretory tests to distinguish type I from type II DM in cats are inconsistent partly because of the effects of glucose-induced desensitization and glucose toxicity. A clinically useful way of distinguishing type I from type II DM in cats may be to evaluate response to treatment with antidiabetic drugs.
conversion of ingested carbohydrate to lactate by the intestinal mucosa, which is subsequently absorbed and metabolized by the liver. Incriminating metformin as the sole cause of all lactate elevations is complicated because obesity and diabetes also slightly raise blood lactate concentrations. The risk of death from metformin-induced lactic acidosis (50%) is similar to that of severe hypoglycemia in sulfonylurea-treated patients.

In most patients suffering from metformin-associated lactic acidosis, predisposing factors include concurrent renal insufficiency, liver disease, or other major illness causing tissue hypoperfusion or hypoxia. The risk of death from metformin-induced lactic acidosis (50%) is similar to that of severe hypoglycemia in sulfonylurea-treated patients.

There are infrequent reports of drug interactions with metformin. In humans, cimetidine causes an elevation of plasma metformin by competition for renal tubular secretion. Cats

There is little information on the adverse effects of metformin in cats. In cats, the drug appears to be excreted primarily by glomerular filtration. The effects of cimetidine on plasma metformin concentration in cats are unknown.

In one study, six healthy male cats received metformin (25 mg sid for 7 days, then 25 mg bid for 14 days) and two cats received placebo. All six cats receiving metformin, but neither cat receiving the placebo, developed a combination of inappetence, weight loss, and/or intermittent vomiting. In another study, six healthy adult cats were given 25 mg metformin IV and PO. There was no mention of adverse effects (e.g., vomiting).

THIAZOLIDINEDIONES (TROGLITAZONE)

Thiazolidinediones were discovered by Japanese scientists almost 2 decades ago as they were studying compounds to serve as hypolipidemic drugs. One analogue, troglitazone, was approved for human use by the FDA in 1997. Troglitazone is rapidly absorbed (its bioavailability is 40% to 50%), and food increases the absorption. In humans, troglitazone undergoes metabolism by sulfation, glucuronidation, and oxidation into active conjugates. Hepatic impairment causes plasma concentrations of troglitazone to increase. Despite proven efficacy, its suitability as a first-line drug to treat type II DM has been questioned because of the risk of severe liver dysfunction.

Like metformin, troglitazone enhances peripheral insulin sensitivity and thereby lowers both glucose and insulin levels. Troglitazone reduces the expression of specific genes responsible for producing the regulatory enzymes of hepatic gluconeogenesis, thereby slowing the rate of hepatic gluconeogenesis. In muscle and fat, thiazolidinediones cause an increase in intracellular glucose transport, which increases glucose metabolism and decreases peripheral demand for insulin. Troglitazone has no effect on insulin production or secretion at the pancreatic beta cell.

Efficacy Humans

Clinical trials show that troglitazone achieves long-term (up to 2 years) glycemic control in humans. To date, six trials examining troglitazone as the sole agent for treating type II DM showed a mean decrease in FBG of 34 mg/dl and in Hb A1c of 0.6%. Therefore, troglitazone is not as efficacious as monotherapy when compared with other classes of antidiabetic drugs.

Primary treatment failure occurs in 25% of humans with type II DM treated with troglitazone alone. Troglitazone is more effective in patients with the syndrome of insulin resistance, where serum insulin concentrations are very high. This is in keeping with the described mechanism of action in peripheral tissues (enhancing insulin sensitivity). Combination therapy with metformin is not recommended because troglitazone and metformin have similar mechanisms of action and do not show complementary effects as do metformin and a sulfonylurea or troglitazone and a sulfonylurea.

Cats

There is no published information on the efficacy of troglitazone in cats.

Side Effects Humans

Troglitazone-related adverse effects occurred in one fourth of patients using troglitazone either as monotherapy or in combination with a sulfonylurea. Liver-related death occurs in 1 of 100,000 humans. This has raised questions regarding the role of troglitazone in the repertoire of antidiabetic drugs; therefore, troglitazone is no longer recommended by the FDA as monotherapy. The causative mechanism of hepatotoxicity is unknown but may represent idiosyncratic injury as a result of aberrant metabolism, resulting in the accumulation of hepatotoxic metabolites.

Troglitazone may cause expansion of the plasma volume; 5% of patients receiving the drug experience edema. Its use is contraindicated in patients with New York Heart Association class III or IV cardiac status.
Cats
There are no published data on adverse effects of troglitazone in cats.

α-Glucosidase Inhibitors (Acarbose)

α-Glucosidase inhibitors delay glucose absorption from the GI tract. Acarbose, an α-glucosidase inhibitor, is an oligosaccharide extracted from the bacterium Actinomyces. It was first developed as a starch blocker for obesity. Acarbose was introduced in the United States in 1995 and has recently been studied for use in domestic animals.40,41

Dietary control of blood glucose through stringent dietary regimens has been the proposed foundation of early therapy for human diabetes, but noncompliance with eating small, frequent meals is high.7,10 Similarly, owners of diabetic cats are often unable to provide small, frequent meals. Appropriate dietary therapy for diabetic cats is outlined elsewhere.19

Acarbose inhibits the α-glucosidases, which include enzymes produced in the brush border of the small intestine. Sucrase, maltase, isomaltase, glucoamylase, lactase, and others function to digest oligosaccharides and disaccharides (complex carbohydrates) into monosaccharides (glucose), which are subsequently absorbed through the small intestine.42 Acarbose competitively and reversibly inhibits these enzymes, delaying the hydrolysis of complex carbohydrates without affecting the absorption of the glucose molecule.10 Carbohydrate absorption then shifts to more distal parts of the intestines.43 Carbohydrates that reach the large intestine are metabolized by colonic bacteria into fatty acids for absorption.

Acarbose does not cause a malabsorptive state; rather, it slows the digestive and absorptive processes. The end result is a blunted entry of glucose into the systemic circulation, thus reaching the pancreatic beta cell at lower blood concentrations.44,45 Acarbose does not decrease hepatic glucose output or reverse any pathophysiologic derangements in patients with diabetes. In fact, the drug is not systemically absorbed.

Efficacy

Humans
Human studies with acarbose have documented a decrease in PPBG concentrations and glucosuria for up to 3 years irrespective of concomitant therapy.10,42,44-48 This occurs in both insulin- and non-insulin-dependent DM, which may have implications for veterinary medicine because discriminating between type I and type II DM would not be a factor in deciding whether or when to prescribe the drug. When used alone in humans, acarbose decreased the FBG level by only 25 to 30 mg/dl, the PPBG level by 40 to 50 mg/dl, and the Hb A1c concentration by 0.5% to 1.2%.49-51 Although less potent than insulin, glipizide, or metformin, acarbose is prescribed as initial and adjunctive therapy in obese patients. Acarbose does not affect the absorption of other antidiabetic drugs. It is not recommended for patients with normal or decreased body condition.50

Cats
The efficacy of acarbose in cats is not established. Because acarbose works by interfering with starch digestion and absorption, its effectiveness needs to be studied in cats in light of their low carbohydrate intake when compared with humans.12 Recently, seven obese diabetic cats (five on insulin therapy) were evaluated for the effects of acarbose (12.5 mg PO bid with meals) and a high-protein diet on glycemic control. Insulin administration was discontinued in four of five cats during the course of the 4-month study. Improved serum fructosamine and FBG concentrations as well as improved attitude compared with pretreatment values were noted in six cats.41

Side Effects

Humans/Dogs

Up to 30% of humans experience mild and transient GI side effects from acarbose that diminish despite continued drug use. Bloating with abdominal discomfort, flatulence, and diarrhea have been reported.45,52-55 In five healthy dogs fed a high-fiber diet and given 200 mg acarbose daily, four dogs developed soft to watery stools and two dogs lost weight during the study.40

To minimize the incidence of GI side effects, acarbose therapy should be initiated with a low dose and gradually increased to reach the minimally effective dose.48 Food must be present in the bowel with acarbose for the drug to have its effect, but side effects may occur regardless of the presence or absence of food.

Other adverse effects are dose dependent and include high liver enzyme activities and abnormal results of liver function tests. These abnormalities resolve when the drug is discontinued. Hypoglycemia does not occur as a direct result of acarbose therapy. However, if hypoglycemia occurs due to concurrent administration of other antidiabetic drugs (insulin, glipizide), pure glucose should be ingested.52-55

Cats
The appropriate dose for cats has not been established.
CONCLUSION

The mechanism of action, efficacy, and side effects of the oral antidiabetic drugs glipizide, metformin, troglitazone, and acarbose have been extensively studied in humans but not in cats. On the basis of limited data, glipizide and acarbose appear to have the most efficacy and the least potential for toxicity when compared with metformin and troglitazone. Careful patient selection is important. Oral antidiabetic drugs may be appropriate for cats that are in good overall health with early or mild clinical signs of diabetes and those with owners who are unwilling or unable to administer insulin injections. There are complications and many uncertainties regarding the current use of oral antidiabetic agents in cats. They should not be used in cats with evidence of diabetic complications (e.g., ketoacidosis, infection, any concurrent disease).

Although the difficulty in differentiating between type I and II DM in cats complicates the ideal treatment plan for each patient, it is clear that not every newly diagnosed diabetic cat requires exogenous insulin. Hyperglycemia in cats with type II DM may be a reflection of impaired insulin secretion from the pancreas, increased hepatic glucose output, decreased peripheral insulin sensitivity, and intestinal glucose absorption. If so, therapy would ideally revolve around correcting these abnormalities by the use of dietary changes, oral antidiabetic agents, insulin, or a combination of these treatments. Some cats that are exquisitely sensitive to insulin may benefit from a diet change and the use of an oral agent without insulin. Other cats that are well maintained with insulin and then become unregulated may represent the progressive nature of type II diabetes; these cats may also benefit from the addition of drugs (e.g., glipizide or acarbose alone or with insulin). More information is needed on the use of combination therapy in cats and the efficacy and/or toxicity of metformin and troglitazone. Initial observations have not been encouraging. The reason for the apparent lack of efficacy compared with that in humans remains unknown but may be related to low serum insulin concentrations associated with glucose toxicity.

Improving recognition of type II DM in cats and further study of oral antidiabetic agents are important for managing the unique characteristics of feline diabetes. To date, clinical trial data are insufficient in both human and veterinary medicine for determining the optimal insulin formulation and optimal combinations and dosages of oral agents. We hope that future research
will provide clues to the many unanswered questions regarding glycemic control in cats.

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1. Which of the following is not a result of glucose toxic-
ity?
   a. desensitization of the pancreatic beta cell to glucose
   b. dysfunctional glucose transport systems in peripheral
tissues
   c. movement of peripheral insulin receptors beneath
   the cell membrane
   d. low serum insulin concentration
   e. depletion of liver glycogen stores

2. Insulin resistance is characterized by _____ serum in-
sulin concentration and _____ blood glucose.
   a. high; low
   b. high; high
   c. low; high
   d. low; normal
   e. low; low

3. The direct physiologic stimulus for insulin secretion
by the pancreatic beta cell is
   a. closing of the ATP–potassium channel.
   b. hypoglycemia.
   c. intracellular calcium influx.
   d. intracellular potassium influx.
   e. opening of the ATP–potassium channel.

4. In humans, the likelihood of response to glipizide is
improved by selecting patients with
   a. mild to moderate hyperglycemia.
   b. marked hyperglycemia.
   c. insulin resistance.
   d. a history of ketoacidosis.
   e. ketonuria.

5. All of the following are reported adverse effects of glipi-
zide therapy in cats except
   a. jaundice.
   b. vomiting.
   c. hypoglycemia.
   d. constipation.
   e. high liver enzyme activity.

6. To which class of drugs does metformin belong?
   a. a-glucosidase inhibitors
   b. biguanides
c. sulfonylureas

d. thiazolidinediones

e. glycosylated proteins

7. Which of the following are mechanisms by which metformin lowers the blood glucose concentration?
   a. improved insulin-induced suppression of hepatic gluconeogenesis
   b. increased stimulation of insulin secretion by the pancreas
   c. enhanced number and activity of glucose transporters into myocytes
   d. increased uptake and oxidation of glucose in adipose tissue
   e. a, c, and d

8. Troglitazone is not commonly used in cats because
   a. clinical trials have shown that it does not lower blood glucose concentrations in cats as it does in humans.
   b. it causes profound hypoglycemia in cats.
   c. it causes renal toxicity in cats.
   d. its efficacy and toxicity in cats is unknown.
   e. it cannot be used concomitantly with insulin.

9. In a study of seven obese diabetic cats evaluated for the effects of acarbose,
   a. insulin administration could not be discontinued in any of the cats due to refractory hyperglycemia during acarbose administration.
   b. the cats did not tolerate acarbose administration due to the metallic taste reported in humans.
   c. serum fructosamine and FBG concentrations were improved compared with pretreatment values in most of the cats.
   d. the drug resulted in complete resolution of clinical signs of DM in all seven cats.
   e. long-term follow up on all seven cats showed glycemic control on acarbose alone after 1 year.

10. Which of the following statements regarding acarbose administration is true?
    a. Acarbose must be taken on an empty stomach in order to have an affect.
    b. Compared with glipizide, metformin, and troglitazone, acarbose has the most profound effect in lowering the blood glucose concentration.
    c. The use of acarbose is not suitable for insulin-dependent DM (type I).
    d. Therapeutic serum concentrations of acarbose are met by tid administration.
    e. GI side effects in humans are usually transient and diminish despite continued use.