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HYPOGLYCAEMIC ACTIVITY OF CINNAMON BARK EXTRACT IN ALLOXAN-INDUCED DIABETIC RATS

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Abstract

Cinnamon bark is widely used as a spice and in traditional medicine for diabetes, and rats made diabetic with alloxan are among the most common systems used to test such claims. This narrative review gathers the published evidence on the hypoglycaemic activity of cinnamon bark extract in alloxan-induced diabetic rats. It describes the chemistry of the bark, the mechanism and pitfalls of the alloxan model, the reported glucose-lowering effects in rodents, proposed mechanisms involving insulin signalling and carbohydrate digestion, and what human trials and safety data add. No new experiments are reported. The evidence is encouraging but heterogeneous, with variable extracts, doses and controls, and the clinical results remain inconsistent.

1. INTRODUCTION

Cinnamon has been used in food and medicine for thousands of years, and a long folk reputation as a remedy for high blood sugar has made it one of the most frequently tested botanical products in diabetes research. The bark of several Cinnamomum species is sold under the single name of cinnamon, and the products differ in chemistry, taste and safety [1, 2]. That detail is easily lost in laboratory reports, yet it matters when results from different studies are compared. A rat given an aqueous extract of one species and a rat given an alcoholic extract of another are not receiving the same treatment. Dosage also deserves care. Traditional use involves a gram or two of powder in food, while laboratory extracts can be concentrated several-fold, so the exposure in an experiment may bear little relation to the exposure of a person who simply adds cinnamon to porridge [1, 3]. Keeping these differences in mind makes the literature easier to read, and it explains many

apparent contradictions between laboratory and clinical findings [4]. The same applies to the vehicle, which may itself affect absorption [1, 5].

Alloxan-induced diabetes in rats is a long-established model for screening anti-diabetic agents. The compound destroys pancreatic beta cells and leaves the animal insulin-deficient and hyperglycaemic, a state that resembles type 1 diabetes more than the type 2 disease for which cinnamon is usually marketed [6, 7, 8]. The model is cheap and quick, which explains its popularity. It is also easy to misuse, and several features of alloxan toxicity can produce results that look like an extract effect when they are not [9]. For a cinnamon extract, the practical question is narrower: does it lower glucose in animals that have lost most of their insulin-producing cells, and if so how? Answering that requires a clean model, a defined extract and sensible controls, none of which can be taken for granted in the published work [8, 10, 11]. The mismatch with type 2 disease is itself worth keeping in mind [12, 13].

This article reviews the published evidence on the hypoglycaemic activity of cinnamon bark extract in alloxan-induced diabetic rats. It is a narrative review, so it reports no new animal work, no new extract preparation and no new measurements. The sections that follow cover the plant and its constituents, the alloxan model, the rodent findings, proposed mechanisms, the human evidence and safety, and the limitations of the field. The main points are collected in table 1 and grouped in fig. 1. Because the title concerns a specific model, the review leans on animal papers where they exist and borrows from other rodent models and from human trials where they do not. Those borrowed findings are labelled as such throughout, so the reader can judge how far each one applies to alloxan diabetes [12, 14, 15]. Where the evidence is thin, the text says so plainly. The emphasis throughout is on what a reader can safely conclude from the published record.

2. CINNAMON BARK AND ITS CHEMISTRY

Four species dominate trade. Cinnamomum verum, often called Ceylon or true cinnamon (the older name is C. zeylanicum), is grown mainly in Sri Lanka, whereas cassia types, namely C. cassia, C. burmannii and C. loureiroi, come from China and Indonesia and make up most of the cheaper material on the market [1, 2]. The inner bark is peeled, dried and either sold as quills or powdered. Studies of glucose control have used both groups, sometimes without stating which, and this lack of identification is one of the first problems in the literature. Even the botanical name is a source of confusion, because older papers use C. zeylanicum and newer ones C. verum for the same plant. Taxonomic clarity matters for pharmacovigilance as well as science, since regulatory and safety assessments are made for named species [2, 16]. Voucher specimens deposited in a herbarium would settle the question, but few reports mention them. Descriptions of the plant part follow classical pharmacognosy [17]. Without that, reproducing a study is guesswork [1, 17].

The volatile oil of the bark is rich in cinnamaldehyde, which gives the characteristic aroma and is often the main constituent, along with eugenol, cinnamyl acetate and linalool in varying proportions [1]. The non-volatile fraction contains polyphenols, including proanthocyanidins and the type-A polymers described in cinnamon extracts, along with tannins and coumarin-related compounds [5, 18]. Extraction solvent determines which of these end up in the preparation. Water extracts are enriched in polyphenols, while ethanol and hexane extracts carry more of the oil [1, 5, 19]. Seasonal and geographic variation, harvest time and storage add to the variability of composition. Cinnamaldehyde in particular is volatile and oxidises to cinnamic acid on exposure to air, so a stored extract can change in potency [1, 5]. These points are routine in pharmacognosy, but they are seldom discussed in pharmacological papers, where the extract is treated as a fixed reagent [17, 19]. Extraction yields also depend on particle size and contact time, details that are often omitted [5, 19]. Recording extraction temperature and duration is therefore as important as naming the solvent, because heat can drive off the volatile oil [1, 5].

Table 1: Published findings relevant to cinnamon bark extract and alloxan diabetes

Topic	Reported finding	Ref.
Alloxan mechanism	Uptake by GLUT2 and redox cycling selectively destroy beta cells	[6, 7]
Model pitfalls	Unstable compound, variable dose response and spontaneous partial recovery	[8, 9]
Bark constituents	Cinnamaldehyde, eugenol and polyphenols vary with species and solvent	[1, 2, 5]
Coumarin content	Much higher in cassia than Ceylon bark; hepatotoxic in sensitive people	[16, 20]
Cinnamaldehyde in rats	Lowered plasma glucose and raised hepatic glycogen in diabetic rats	[15]
Cinnamon extract in mice and rats	Improved glucose tolerance and insulin-regulated glucose uptake	[14, 21]
Insulin signalling	Polyphenol polymers and a chalcone mimic insulin action in cells	[18, 22, 23]
Digestive enzymes	Extracts inhibit alpha-glucosidase and alpha-amylase in vitro	[24]
Randomised trials	Results inconsistent between trials; small effect on fasting glucose in some	[12, 25, 26]
Systematic reviews	Insufficient evidence for recommendation; high heterogeneity	[27, 28, 29]

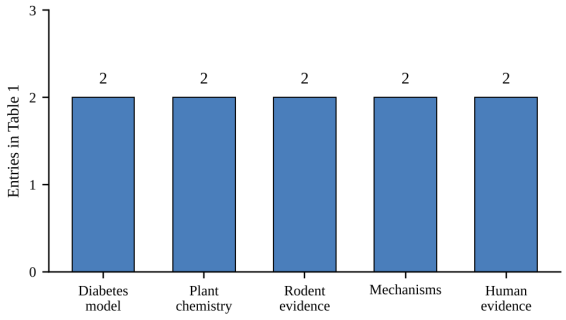


Fig. 1: Number of entries in table 1 by evidence group

Coumarin deserves a separate mention. Cassia bark contains markedly more coumarin than Ceylon bark, and the content in retail cassia has been found to vary widely between samples [16]. Coumarin is hepatotoxic in sensitive people at doses not far above a tolerable daily intake, so an extract that appears to lower glucose in rats but contains much coumarin is not necessarily a good lead for human use [16, 20]. Standardisation, by chemical markers such as cinnamaldehyde and by coumarin content, is rarely reported in the animal studies that form the main evidence here [1, 5]. None of this means that cassia bark should be avoided in research. Cassia is the material most people in many countries actually consume, and trials with it are relevant to real use. The point is that the material must be named, characterised and its coumarin load stated, so that benefit and risk can be weighed together [16, 20, 30]. Safety data should travel with efficacy data [16, 20].

Phytochemical screening is generally performed using classical qualitative tests for alkaloids, flavonoids, tannins, saponins and glycosides, as described in standard pharmacognosy texts [5, 17, 19]. These tests are inexpensive and useful for confirming the presence of broad classes, but they cannot identify individual compounds or quantify them, so they offer little help in explaining activity or in reproducing a preparation elsewhere [5, 19]. Standard references recommend recording organoleptic features such as colour, odour and fracture of the bark, together with microscopy and ash values, as a basic identity check before extraction begins [17, 19]. These simple steps are rarely mentioned in pharmacological reports and could be added at almost no cost. Chromatographic fingerprints, by thin-layer chromatography or HPLC against reference markers such as cinnamaldehyde, go a step further and let a later reader confirm that two batches resemble each other [5, 19]. Screening alone is a starting point.

3. THE ALLOXAN MODEL

Alloxan is a hydrophilic, unstable pyrimidine derivative that is taken up by beta cells through the glucose transporter GLUT2. Inside the cell, it and its reduction product dialuric acid take part in a redox cycle that generates superoxide radicals, which are converted to hydrogen peroxide and then to highly reactive hydroxyl radicals [6, 7]. Beta cells have low antioxidant defences, and the combined oxidative damage and a rise in

cytosolic calcium cause selective necrosis [6, 7]. The result is a rapid fall in insulin secretion. It is this selective uptake that gives alloxan its specificity, and compounds that compete with glucose for GLUT2, or that scavenge radicals, can protect beta cells if given in time [6, 7]. An extract that appears to prevent diabetes may therefore simply be blocking the toxin, which is a quite different claim from lowering glucose in established disease [31]. Cell death then follows within hours [6, 7].

A single dose given intraperitoneally or intravenously to fasted rats is the usual procedure, with doses in the region of 100 to 150 mg per kilogram commonly cited, although the dose that produces stable diabetes without excessive mortality depends on strain, age, route and fasting [8, 9]. Blood glucose follows a characteristic course. There is a brief rise, then a hypoglycaemic phase when damaged cells release stored insulin, which can be fatal unless glucose is provided, and then a sustained hyperglycaemia as the beta cell mass is lost [6, 9]. Animals are generally given glucose solution after injection to prevent fatal hypoglycaemia, and body weight, food and water intake are recorded because diabetic rats lose weight and drink heavily [8, 9]. Deaths in the first days are common at higher doses, and the exclusion of such animals should be reported to avoid survivor bias [9, 11]. The characteristic triphasic response is a useful check that the model has worked as expected [6, 9]. Rats that do not become diabetic, or whose glucose later falls spontaneously, need clear exclusion criteria set in advance [8, 9].

Several pitfalls follow. Alloxan breaks down within minutes in solution, so the preparation and timing of injection affect the dose that actually reaches the animal [9]. Some beta cells may survive, and spontaneous partial recovery of insulin secretion has been described in the weeks after injection, so a fall in glucose over time in treated animals could reflect regeneration and not drug action [6, 8, 9]. Without a diabetic control group followed for the same period, such recovery cannot be separated from a real treatment effect [8, 10]. A reasonable design therefore confirms diabetes before treatment, allocates animals to groups by blood glucose to balance baseline severity, and monitors a diabetic control for the full duration. These steps are standard in rigorous work, though they are not universal in the cinnamon literature [10, 11]. Reviewers should look for these details when assessing a paper [10, 11].

Alloxan also damages the kidney and liver in a dose-dependent way, and it is a relatively unpredictable diabetogen compared with streptozotocin, which has a more stable action but similar caveats [6, 10]. Neither model reproduces the insulin resistance of type 2 diabetes. Since the clinical case for cinnamon is built mostly on insulin sensitisation, the alloxan rat is a partial test at best of the proposed benefit, though it can show whether an extract has insulin-independent or insulin-mimetic effects [8, 13, 21]. Insulin-sensitising effects, the most appealing claim for cinnamon, are best examined in models that retain some insulin secretion, such as high-fat diet combined with a low dose of streptozotocin, or genetically diabetic mice [8, 14]. Total beta cell loss limits what an insulin sensitiser can do. Streptozotocin shares some of these features and offers a useful comparison [6, 10].

Diabetes in these animals is usually defined by fasting glucose above a threshold, commonly around 200 mg per decilitre, measured 48 to 72 hours after injection. Blood glucose is determined by the glucose oxidase method or a glucometer [13, 32]. Because glucometers vary in accuracy at high readings, enzymatic methods on plasma are preferable when results will be compared across studies [32]. Measuring plasma insulin or C-peptide at the end of a study would show whether any glucose fall is accompanied by higher insulin, which would suggest beta cell recovery, or by unchanged insulin, which would point toward an extra-pancreatic action [6, 33]. Without it, two studies can hardly be compared.

4. EXPERIMENTAL EVIDENCE IN RODENTS

Several groups have reported that oral cinnamon extracts or their constituents lower blood glucose in diabetic rodents. Cinnamaldehyde given to

streptozotocin-diabetic rats reduced plasma glucose and glycosylated haemoglobin and was associated with increased hepatic glycogen and plasma insulin, a pattern consistent with improved glucose utilisation [15]. In db/db mice, a cinnamon extract lowered fasting glucose and improved glucose tolerance, and an extract given to normal rats increased insulin-stimulated glucose uptake in muscle [14, 21]. Effects were generally seen at doses of tens to hundreds of milligrams per kilogram, which for a crude extract is a considerable amount and implies high intake if translated to a person [14, 15]. Studies that compare a pure compound with the whole extract are valuable because they show whether a single constituent can account for the activity [3, 15]. Differences in route and vehicle may also contribute [14, 21]. Whether the same effect would be seen with aqueous bark extract in alloxan animals is plausible but is not shown by these particular studies [14, 15].

Reports using alloxan itself follow the same general pattern, with extracts of cinnamon bark reported to reduce fasting glucose compared with untreated diabetic animals and sometimes to improve lipid measures and body weight. Typical designs compare normal controls, diabetic controls, diabetic rats given a reference drug such as glibenclamide, and diabetic rats given graded doses of extract by oral gavage for periods of two to four weeks [1, 8, 10]. The shape of the reported effects is dose related in some papers and flat in others, and the size is modest in comparison with the reference drug [1, 14, 15]. Reductions in cholesterol and triglyceride in treated diabetic rats are reported in some papers and support a wider metabolic benefit, but others show no change, and lipid data are rarely the primary outcome [1, 3, 12]. Histology of the pancreas, when included, sometimes suggests partial preservation or regeneration of islets, which is an interesting observation that needs to be separated from spontaneous recovery by suitable controls [6, 9]. Such secondary outcomes need adequate power to be interpretable [11, 33].

Methodological quality is uneven. Many studies use groups of five or six animals, do not describe randomisation or blinding, and do not report the stability of diabetes before treatment started. Weak design and selective publication are known to inflate apparent efficacy in animal studies, and cinnamon papers are unlikely to be an exception [11]. Extract identity, the method of preparation and the yield are often vague, and the extract dose is expressed per kilogram of body weight with no equivalent in terms of the raw bark [1, 5, 11]. Statistical analysis is another weak point. Multiple group comparisons require appropriate post-hoc tests, and the reporting of individual animal data would allow readers to judge variability. These issues are not special to cinnamon, but they affect how much confidence can be placed in modest effects [11, 33]. Plain reporting of the raw data is a low-cost improvement [11]. Sample size calculations are almost never given.

Design choices deserve a short comment of their own. Allocating animals to groups by random number, and randomising the order of dosing and sampling, protects against the quiet bias that creeps in when the more obviously diabetic animals end up in the treated group [11, 34]. Blinding of whoever measures glucose or scores pancreatic sections is cheap and easily described. Group size is the weaker point. Five animals per group can detect only large differences, and with the wide variation in alloxan response a null result from such a design says very little [9, 34]. Commentators on preclinical research find these items missing from a large share of papers [34]. A study that meets them is not automatically right, but it is easier to believe.

Table 1 brings together representative findings from the sources discussed in this review, covering the model, the chemistry, rodent and human evidence and safety, and fig. 1 shows the number of entries in each group. The imbalance is revealing. There is far more mechanistic and clinical literature than there is rigorous animal work using alloxan and a defined cinnamon extract [8, 12, 14, 27]. In particular, the evidence on cinnamaldehyde is better developed than that for crude bark extracts, and clinical evidence is more extensive than controlled alloxan work. These imbalances should temper any

broad claim about the effectiveness of cinnamon [15, 27]. Readers should keep this imbalance in mind when interpreting the figure.

Antioxidant activity is frequently measured alongside glucose, because oxidative stress underlies both beta cell loss in the alloxan model and diabetic complications. Spices including cinnamon show strong free radical scavenging in vitro, and diabetic tissues show raised lipid peroxidation, so a protective effect is plausible, although antioxidant capacity in a test tube does not prove protection in a living animal [31, 35]. Such measurements are not complicated, but they require stored plasma and suitable assay kits, and many small studies lack both. Bringing them into standard protocols would add real mechanistic value [32, 33]. It also guards against over-reading a single result. Samples should be stored frozen, and the interval between sampling and assay stated, since lipid peroxidation products drift on storage [31].

The choice of reference drug also shapes interpretation. Glibenclamide, the usual comparator, stimulates insulin release and so depends on surviving beta cells. In a rat with severe alloxan damage it may perform poorly, and an extract that appears to match it has not necessarily done anything remarkable [6, 8]. Metformin or insulin are used as comparators in some laboratories and act largely independently of beta cell mass, which makes them more informative positive controls [8, 10]. Whichever is chosen, its dose and timing should be reported [9, 10].

5. PROPOSED MECHANISMS

The best-known mechanism concerns insulin signalling. A water-soluble polyphenol fraction from cinnamon, described as type-A polymers, enhanced insulin-dependent glucose metabolism in adipocytes, and a hydroxychalcone from the bark acted as an insulin mimetic [18, 22]. Fractions of the bark also inhibited protein tyrosine phosphatase-1 and increased insulin receptor kinase activity in cell-free systems, which would amplify the signal downstream of the receptor [23]. In rats, a cinnamon extract was reported to improve insulin-regulated glucose utilisation through increased insulin receptor signalling in muscle [21]. The case for such a mechanism is strongest in cultured cells, and the doses used in these systems are not easily compared with what reaches tissues after oral dosing. Absorption, metabolism and the form of the active constituents in plasma are largely uncharacterised for the polyphenol polymers [18, 21, 23]. Without those data, mechanism remains a hypothesis. Insulin-mimetic activity of this kind would be relevant even in animals with few beta cells [21, 22].

A second possible mechanism involves digestion. Extracts of several cinnamon species inhibit intestinal alpha-glucosidase and pancreatic alpha-amylase in vitro, and the effect was additive with acarbose in the study that tested the combination [24]. Slower carbohydrate digestion would blunt the post-meal rise in glucose, a mode of action that does not depend on insulin and might therefore operate in an alloxan rat [3, 24]. Delayed gastric emptying has also been proposed, on the basis of human data, but it is not well established [3, 36]. Intestinal enzyme inhibition has the attraction of acting inside the gut lumen, where the extract is present at high concentration. It does not, however, explain effects on fasting glucose, which are the usual outcome in rat studies and in several trials [24, 36]. The mechanism may be real, but its contribution to the glucose lowering seen in animals measured after fasting is likely to be limited [3, 36]. Studies in diabetic rats are needed to test it directly [3, 36]. Acarbose, a licensed alpha-glucosidase inhibitor, provides a benchmark for how strong the effect would need to be to matter clinically [3, 24].

Several less-tested ideas exist. Cinnamaldehyde may influence glucose transporter expression and hepatic glucose output, and it is reported to improve lipid profile in diabetic rodents [3, 15]. The antioxidant properties of the bark could protect surviving beta cells, which might partly explain results in alloxan animals if the extract is given before the toxin [31, 35]. Each of these proposals is supported by a handful of experiments, and most are in vitro or in other species. Their relative importance

in vivo is unknown [3, 4]. A fair summary is that cinnamon may act through several modest effects at once, none of which has been shown to dominate. That is common for plant extracts, whose complexity is both a strength and a weakness. It also means that a reliable standardised extract is more important than a single marker compound [3, 5]. Clear reporting of the extract composition would allow progress [5].

6. CLINICAL EVIDENCE AND SAFETY

Human trials give a more mixed picture than the animal work. An early placebo-controlled trial in Pakistani adults with type 2 diabetes reported falls in fasting glucose, triglycerides and cholesterol after cinnamon capsules, but later trials in other populations did not reproduce the effect on glycated haemoglobin [12, 25, 26]. A cassia extract improved fasting glucose in a German trial, while other trials found no benefit [25, 26]. Differences in species, dose, duration and background therapy make the discrepancy difficult to resolve [4, 30]. Trial populations differ in baseline glycaemia, with greater effects tending to appear when glucose control is poor. Cinnamon is generally added to existing drugs, so any extra benefit has to be detected on top of effective therapy, which is statistically demanding [4, 30, 37]. Short-term studies in healthy volunteers have also failed to show consistent changes in glucose tolerance [36]. Differences in response between individuals are also large [26, 37].

Systematic reviews have reached cautious conclusions. A Cochrane review found insufficient evidence to recommend cinnamon for diabetes, mostly because trials were small, short and of uncertain quality [28]. Meta-analyses of randomised trials have reported small reductions in fasting plasma glucose, but with high heterogeneity and little effect on glycated haemoglobin [27, 29, 38]. Reviewers have also pointed to the likelihood of publication bias and to inconsistent reporting of the species used [3, 30, 37]. Pooling studies that differ so much in species, dose and duration is itself a source of concern. Sensitivity analyses that remove low-quality trials generally reduce the apparent effect, which is a common pattern when evidence is weak [27, 28, 29]. For this reason, current guidelines do not include cinnamon among recommended therapies [13, 28]. The overall message is cautious rather than negative [27, 28].

The choice of outcome affects what trials can show. Glycated haemoglobin reflects glucose exposure over roughly two to three months, so a trial lasting four to six weeks has little chance of moving it, whereas fasting glucose responds sooner but fluctuates from day to day [27, 29]. Some of the early positive trials leaned on fasting glucose, while several later trials took glycated haemoglobin as the main measure, which may account for part of the disagreement [12, 25, 26]. A fair comparison needs trials of at least three months that report both [28, 37].

Safety needs to be set beside efficacy. Cinnamaldehyde is generally well tolerated at food levels, but cassia preparations contain coumarin, and regular high intake could exceed the tolerable daily intake set by European risk assessors, with liver injury reported in sensitive individuals [16, 20]. In rodent studies the standard acute and repeated-dose toxicity protocols provide a structure for assessing extract safety, yet most efficacy papers do not include them [39, 40]. Interaction with glucose-lowering drugs is plausible and has not been well studied [4, 30]. Practical advice for patients is straightforward. Cinnamon as a spice is safe for most people, but supplements of cassia in high doses should be avoided in those with liver disease or on hepatotoxic medicines, and cinnamon should never replace prescribed treatment [16, 20, 28]. Clinicians should ask about supplement use, since people often do not mention it [4, 30]. Such advice is consistent with the available evidence [16, 30]. Case reports of liver injury linked to cinnamon supplements are few, but they are consistent with the coumarin concern [16, 20].

A final point concerns the use of the animal results to support human use. Diabetes in humans is a chronic disease with complex metabolic dysregulation, and a short-term glucose-lowering effect in a toxin-induced rodent does not predict clinical value without adequate pharmacokinetic and dose translation. Allometric scaling from rat to

human doses is seldom reported [3, 8]. Dosage conversion between species is usually done on a body surface area basis rather than body weight, and this can change the apparent human equivalent several-fold [8, 39]. Journals could require it routinely, with the human equivalent dose stated beside the animal dose so that readers can see at once whether the exposure is realistic [8, 39].

7. LIMITATIONS AND FUTURE DIRECTIONS

The limitations of the evidence are clear. Extract identity and standardisation are poor, animal group sizes are small, controls and randomisation are often not described, and the alloxan model has features that complicate interpretation, including spontaneous recovery and variable severity [8, 9, 11]. Few studies report toxicity, and fewer still follow animals long enough to show durable control [39, 40]. In humans, trials have been short and heterogeneous, and reviews disagree on the size and clinical importance of the effect [27, 28, 29]. These weaknesses are not unique to cinnamon, and similar reviews of other botanical antidiabetic candidates report the same pattern of promising early work followed by disappointing replication. The field would benefit from agreed minimum reporting standards for plant extract studies [1, 11]. Larger, better designed studies are therefore needed [8, 11]. A narrative review can describe these issues but cannot resolve them [8, 11].

Better work is within reach. Studies should specify the species, plant part, voucher specimen, solvent, yield and chemical markers including coumarin, and should report randomisation, blinding and sample size [1, 11, 16]. They should include diabetic controls followed for the same period, a reference drug, and several doses, and should measure insulin where possible so that the mechanism can be examined [10, 32, 33]. Positive results then deserve replication by an independent group before any clinical claim is made [3, 4]. Funding agencies and journals can help by requiring authentication of materials and by valuing replication and negative results. Without that, the literature will continue to accumulate small positive reports of uncertain value [3, 4]. Registration of preclinical protocols is one possible step in this direction [11].

8. CONCLUSION

The literature supports the idea that cinnamon bark extracts can lower blood glucose in diabetic rodents, including those made diabetic with alloxan, and several plausible mechanisms have been proposed, from insulin signalling to inhibition of digestive enzymes [14, 18, 23, 24]. The strength of that evidence is limited by poorly defined extracts, small groups and the quirks of the alloxan model, which make it hard to separate drug effect from spontaneous recovery [8, 9, 11]. Whether the same applies to a standardised extract in a well-controlled alloxan study remains to be shown.

In human beings, trials and reviews do not yet justify using cinnamon as a treatment for diabetes, and safety issues such as coumarin deserve attention [16, 20, 27, 28]. For research, the priorities are clear: authenticated, standardised extracts, proper controls, mechanistic measurements and independent replication. For practice, cinnamon is best regarded as a food flavouring with possible, unproven benefit, not as a substitute for established therapy [28, 30]. That position may change if well-designed studies appear.

9. ABBREVIATIONS

GLUT2-Glucose transporter 2, HbA1c-Glycated haemoglobin, OECD-Organisation for Economic Co-operation and Development, PTP-1-Protein tyrosine phosphatase-1, ROS-Reactive oxygen species, db/db-Leptin receptor-deficient diabetic mouse, i.p.-Intraperitoneal, HPLC-High-performance liquid chromatography

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Nil

11. AUTHORS CONTRIBUTIONS

All the authors have contributed equally.

12. CONFLICT OF INTERESTS

Declared none

13. REFERENCES

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