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REVIEW ARTICLE

The impact of AGEs on human health and the development of their inhibitors based on natural compounds

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Abstract Advanced glycation end products (AGEs) are a heterogeneous group of complex chemical entities resulting from non-enzymatic reactions between reducing sugars with proteins, lipids and/or nucleic acids. AGEs tend to accumulate in cells and stimulate diverse signaling pathways that are closely related to the emergence of several chronic metabolic disorders. This review is based on keywords "medicinal plant", "AGEs", "AGEs complication", "AGEs inhibitor" and their characteristics. The keywords are widely identified and checked in databases such as Science Direct, PubMed Medline, Scopus, and Google Scholar. The complex processes of AGEs formation and their impact on human health are reviewed along with recent developments in AGEs inhibitors derived from natural compounds. In addition, the mechanisms of action of natural inhibitors such as quercetin, lignan, chlorogenic acid, resveratrol and stilbenes are summarized in the protection of glycation-sensitive sites in proteins, removal of active carbonyl compounds, chelating metal ions, and reduction of blood glucose levels. Despite showing glycation-induced-free radicals scavenging activity, these compounds have not yet been widely used in clinical field. Therefore, such natural compounds with specific molecular frameworks might have great potential to pave the way of

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new drugs discovery.

1. Introduction

Advanced glycation end products (AGEs) are a group of diverse compounds that are produced in the degenerative phase of non-enzymatic glycation of biological macromolecules (Song et al., 2021). The chemical reactions leading to non-enzymatic glycation involve the interaction between the active carbonyl groups of reducing sugars and the free amines of proteins, lipids and nucleic acids. AGEs are highly destructive and have a significant potential to endanger human health (Byun et al., 2017, Dong et al., 2023). In vitro studies have shown that protein-AGEs can significantly change the function, secondary structure, and biological activities of proteins, which ultimately leads to cell damage and death (Oshitari 2023). In addition, AGEs participate in the regulation of a series of signalling pathways, such as the transcriptional activator (STAT), nuclear transcription factor (NF-κB), and mitogen-activated protein kinase (MAPK) pathways. AGEs have been implicated in the pathogenesis of metabolic disorders, including atherosclerosis, diabetes, and Alzheimer's disease (Kim et al., 2023, Lyu et al., 2023).

Reducing and inhibiting endogenous AGEs is one of the strategic goals in the prevention and control of diabetes (Tian et al., 2023). For example, metformin, an antidiabetic drug, helps reduce the concentration of methylglyoxal (MGO), an important precursor of AGEs, by lowering blood glucose levels and stimulating the activity of glyoxalase I (GLO1) (Laus et al., 2023). Aminoguanidine selectively suppresses AGEs by removing reducing carbonyl groups and acting as scavengers of α-dicarbonyl compounds. However, its clinical application is limited due to unavoidable side effects. Therefore, a suitable alternative based on Natural compounds, while abundant in nature, with complex and diverse molecular frameworks, can be introduced as effective candidates (Khan et al., 2020, Jia et al., 2022). Since natural medicines have diverse pharmacological and physiological activities, the identification and analysis of their compounds provides a suitable platform for the development of new AGEs inhibitors (Dariya and Nagaraju 2020, Sadeghi et al., 2022).

It is believed that the bioactive compounds from medicinal plants such as polyphenols, flavonoids, alkaloids, terpenoids and other phytochemicals with strong antioxidant and anti-glycation properties might have potential to suppress or reduce oxidative stress and cell damage caused by glycosylation (Fecka et al., 2022). This mini-review has collected recent reports about the anti-glycation mechanism of selected herbal and synthetic compounds (Table 1). The theme is to furnish pharmacology researchers with a more comprehensive understanding of potential treatment options aimed at reducing harmful effects of diabetes and other conformational diseases. By elucidating the complex biochemical pathways that can be inhibited by these agents, it is hoped that efforts to develop drug strategies will be successful.

1.1. Databases search evaluation

A comprehensive and systematic review of the protective properties of antioxidants derived from medicinal plants against the destructive process of producing AGEs is facilitated by searching a set of databases. A detailed search using keywords such as "AGEs", "AGEs effects", "antioxidants", "herbal medicine" is possible in databases such as Science direct, PubMed Medline, Scopus and Google Scholar. These multimodal databases provide valuable insight into the potential therapeutic and protective potential of antioxidant-rich medicinal plants against AGE adducts and their deleterious threats to human health.

1.2. Content gathering

The role of bioactive molecules against the non-enzymatic process of glycation was performed by comprehensive screening of 70 articles containing the keyword "antidiabetic" and 67 articles with the keyword "glycation". The focus was on compounds derived from medicinal plants and their role in inhibiting the non-enzymatic glycation process leading to the formation of AGE adducts (Chinchansure et al., 2015). The analysis of most of the selected articles showed that AGEs play an important role in the pathogenesis of several chronic diseases, including diabetes, cancer, and Alzheimer's disease. The interaction between AGEs and their receptors (RAGEs) has also been identified as a key factor in the occurrence and prevalence of pathological conditions. Both synthetic and natural inhibitors were investigated. In addition, any duplicate content was carefully removed from the analysis process, ensuring that only unique and relevant studies were included in the final selection. Accordingly, potential preventive mechanisms that could be based on medicinal plant ingredients in order to suppress or inhibit AGE adducts and their downstream effects are introduced.

1.3. Path of AGEs formation

In the realm of biochemical processes, there exist two noticeable rout for the generation of AGE adducts, which demonstrate the intricate interplay between oxidative and glycation processes. The initial pathway entails the oxidation of glucose when subjected to metallic ions (Fig. 1), resulting in the production of a radical ketoaldehyde. Upon interaction with the amino groups (–NH2) intrinsic to proteins, the ketoaldeyhde undergoes a chemical reaction, thereby forming ketominin, an important intermediate that ultimately contributes to the formation of AGEs. In the alternative route, amadori products are autoxidized, thereby producing reactive superoxide species, which eventually give rise to AGEs (Chinchansure et al., 2015). It is notable that free radicals are renowned for their high reactivity due to their possession of unpaired electrons. The deleterious impacts of free radicals are well-known in the scientific community and have been extensively studied. These reactive species possess an unpaired electron, which makes them highly unstable and prone to cause damage to biological macromolecules such as proteins, lipids, and nucleic acids. The resultant alterations in the function of these macromolecules can lead to cell dysfunction, tissue damage, and a range of pathological conditions (Upadhyay et al., 2014).

In diabetic individuals, the production of free radicals is observed to be significantly elevated due to various metabolic dysregulations. Consequently, this leads to a cascade of damaging events that weaken the antioxidant defense systems of cells, including impairment of enzymatic and non-enzymatic antioxidant mechanisms. This imbalance between oxidant and antioxidant levels can trigger the onset and progression of various chronic complications associated with diabetes, including nephropathy, neuropathy, retinopathy, and cardiovascular disorders (Fecka et al., 2022).

To mitigate the harmful effects of free radicals in diabetic patients, the use of antioxidants has gained significant attention in recent years. Antioxidants are natural or synthetic molecules that can neutralize free radicals by donating electrons, halting their chain reaction, and thus preventing further damage to macromolecules. Interestingly, several studies have reported the antioxidant properties of various plant-derived substances, making them promising candidates for the prevention and treatment of diabetic complications (Sahu et al., 2023). In a

Table 1 List of some medicinal plants containing bioactive ingredients which represent antioxidant and antiglycation activities along with related physiological functions.

S. NO.	Family	Herbs noun	Functional
1	Theaceae	*Camellia nitidissima*	Inhibited the AGEs formation by scavenging methylglyoxal (Wang et al., 2016).
2	Asteraceae	*Calendula officinalis*	Stopping the Maillard reaction and preventing oxidation *in vitro* (Ahmad et al., 2012).
3	Juglandaceae	*Juglans regia*	Inhibition of early and intermediary AGEs at different incubation conditions (Atta et al., 2023).
4	Asteraceae	*Erigeron annuus*	Exploring the metal-chelating efficacy, reduced binding affinity of AGEs to the receptor, hemoglobin (Hb) and protective capabilities against fructose-induced damage (Jang et al., 2008).
5	Ericaceae	*Empetrum nigrum*	Inhibition of AGEs accumulation and ROS dicarbonyl trapping (Khan et al., 2020).
6	Vitaceae	*Vitis vinifera*	Trapping methylglyoxal and inhibitory effect on BSA glycation (Yoon and Shim 2015).
7	Rosaceae	*Crataegus laevigata*	Suppression carboxymethyl lysine and decrease LDL cholesterol (Sadeghi and Miroliaei 2022).
8	Asteraceae	*Anthemis nobilis*	Protective capabilities against fructose-induced damage (Nagai et al., 2010).
9	Saururaceae	*Houttuynia cordata*	Trapping methylglyoxal (Yoon and Shim 2015).
10	Lamiaceae	*Origanum majorana*	Inhibited the formation of MGO, blocking conversion of dicarbonyl intermediates (Starowicz and Zieliński 2019).
11	Cyperaceae	*Cyperus rotundus*	Inhibiting the oxidative processes (Ardestani and Yazdanparast 2007).
12	Amaryllidaceae	*Allium cepa*	Protection of formation BSA-fructose *in vitro* (Pradeep and Srinivasan 2018).
13	Schisandraceae	*Llicium religiosum*	Decrease of BSA-glycation (Khan et al., 2020).
14	Lamiaceae	*Origanum officinalis*	Inhibit BSA-AGE, and HbA_1c production, reducing protein glycation and MGO rate in diabetic rate (Peng et al., 2011).
15	Polygonaceae	*Fagopyrum esculen*	Strong antyglycation activity due of having strong antioxidant activity (Khan et al., 2020)
16	Fabaceae	*Sophora flavescens*	Inhibition activity of AGEs development (Peng et al., 2011).
17	Lauracae	*Cinnamomum zeylanicum*	Inhibition activity of AGEs development (Talaei et al., 2017)
18	Lamiaceae	*Thymus vulgaris*	Mitigation of methylglyoxal biosynthesis through suppression strategies (Jang et al., 2008).
19	Asteraceae	*Chrysanthemum morifolium*	Inhibit the fluorescent AGEs formation and N-carboxymethyllysine in *in vitro* (Ho et al., 2014).

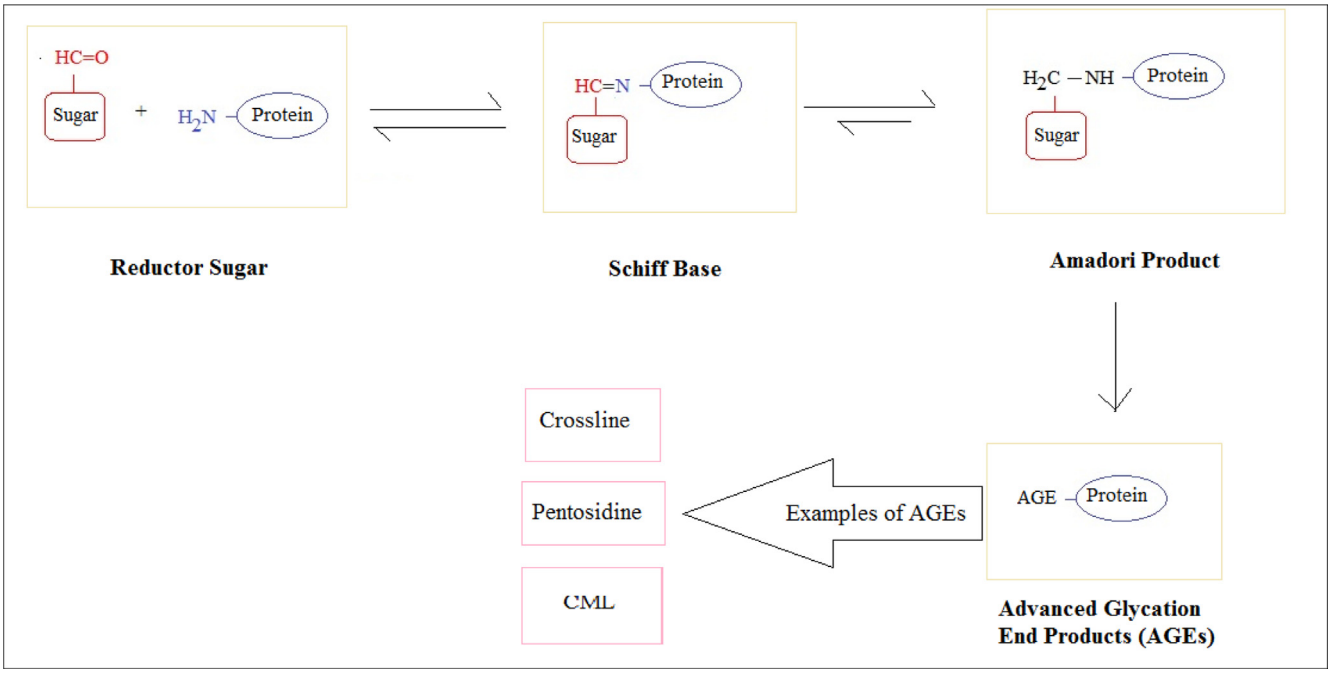

Fig. 1 The visual depiction of advanced glycation end-product formation is being presented.

study conducted on plants selected based on their putative antioxidant activity, it was found that the majority of them possessed potent antioxidant properties. As a result, these plants may hold significant therapeutic potential for diabetic patients as they can potentially counteract the deleterious effects of free radicals and restore the redox balance within cells. Therefore, interventions with antioxidant-rich plant extracts could serve as a valuable adjuvant approach for managing diabetic complications.

There are two significant methods for AGEs productions, which illustrate the communication between oxidation and glycation; in the first stage, oxidation of glucose in the presence of metal ions leads to the formation of radical ketoaldehyde. After ketoaldehyde reaction with the $-NH_2$ groups of proteins, ketominin is formed and leads to the production of AGEs (Chetyrkin et al., 2011). The second method involves the autoxidation of amadori products, which are eventually produced AGEs and radical superoxide. Free radicals are extremely reactive because they contain uncoupled electrons (Valko et al., 2007). Thus, free radicals damage macromolecules and alter their function. In diabetics, the free radicals produced lead to damage to macromolecules and the weakening of antioxidant systems. Therefore, antioxidants can play an important role in preventing chronic complications of diabetes (Goodarzi and Zal 2006). Most of the plants selected in this study had antioxidant properties.

1.4. Assessing the impact of AGEs on protein

AGEs can have very harmful effects and cause diseases in the body. These effects directly on the protein, causing changes in its structure or binding to the RAGEs, activating cascading pathways and abnormal reactions in the cell. The process of glycation, is known to have a multitude of effects on various aspects of protein function. It has been observed that glycation can alter the catalytic activity of enzymes, leading to changes in their substrate specificity and turnover rates. Additionally, glycation can result in the formation of crosslinks between proteins, which can have significant consequences for their structural integrity and stability (Chetyrkin et al., 2011). Moreover, glycation has been shown to induce the production of free radical scavenging centers within proteins, which may confer some protective benefits against oxidative damage. However, the formation of such centers can also lead to altered chemical reactivity and potential loss of function of the protein. Another consequence of glycation is the reduction of binding affinity of ligands and regulatory molecules to their target protein. This may result in altered signaling pathways or impaired cellular response to external stimuli. Notably, these effects of glycation are not limited to a specific subset of proteins or enzymatic reactions, but rather are observed across a wide range of biological systems. The precise mechanisms underlying these effects remain an active area of research, as does the development of strategies to mitigate the detrimental consequences of glycation in both health and disease, some of which are discussed below.

1.5. Exploring the effects of AGEs on enzymatic activity

The phenomenon of enzyme inactivation has been extensively studied in biochemistry, and it is widely accepted that the most probable mechanism leading to this outcome involves the binding of glucose molecules to the epsilon-Lysin amine group located at the active site of the enzyme. The implications of such an interaction can be exceptionally significant, particularly when considering the role played by the epsilon-Lysin residue in catalytic activity. When the aforementioned residue is targeted and rendered inactive through glycation or similar processes, the overall functionality of the enzyme in question is substantially compromised (Tabassum et al., 2020).

Among the plethora of enzymes that are susceptible to this mode of inactivation, Lecithin cholesterol acyltransferase (LCAT) stands out as being one of the most crucial. Indeed, glycation of LCAT can result in a significant loss of its essential fat function, which is responsible for facilitating the transfer of cholesterol from peripheral tissues back to the liver. This impairment of LCAT activity can lead to the accumulation of cholesterol in peripheral tissues, ultimately resulting in the development of atherosclerotic lesions and subsequent cardiovascular disease. Therefore, elucidating the underlying mechanisms of LCAT glycation and investigating potential therapeutic interventions aimed at mitigating this process may represent a critical avenue for future research efforts aimed at combating cardiovascular disease (Low et al., 2012).

1.6. Mechanisms underlying the impact of AGEs on free radical production

AGEs, have been shown to accumulate in the body over time. AGEs have been implicated in a variety of pathological conditions, including diabetes, Alzheimer's disease, and cardiovascular disease (Salami et al., 2023). One of the key mechanisms by which AGEs exert their deleterious effects is through the production of active sites that exhibit Enzyme-like Properties, commonly referred to as Nanozymes. These Nanozymes can catalyze one-electron reduction reactions, leading to the generation of free radicals. The ability of these active sites to facilitate such reactions arises from the presence of certain functional groups, such as amino acids, that are capable of generating reactive intermediates upon exposure to certain types of radiation or other forms of energy. Such intermediates can then react with molecular oxygen to produce highly reactive species, such as superoxide anion, hydrogen peroxide, and hydroxyl radical, all of which are known to contribute to oxidative stress and damage (Bauer et al., 2022).

In addition to their catalytic activity in one-electron reduction reactions, AGE-derived Nanozymes can also catalyze the oxidation reactions of metal-like species, such as iron and copper. This is achieved through the formation of Schiff base products, which can interact with metal ions to promote electron transfer reactions that lead to the generation of reactive oxygen species (Wei et al., 2023). These processes can have profound implications for cellular function and may contribute to the development of various inflammatory diseases and cancer. Overall, understanding the mechanisms underlying the formation and properties of AGE-derived Nanozymes is of paramount importance in elucidating the pathogenesis of various chronic diseases and developing targeted therapeutic interventions aimed at mitigating the harmful effects of oxidative stress (Gui et al., 2023).

1.7. Insights into the molecular mechanisms underlying the effects of AGEs through binding to receptor for advanced glycation end products (RAGEs)

The binding of AGEs to RAGEs triggers a cascade of intracellular signaling events that culminate in the activation of multiple transcription factors, including nuclear factor-kappa B (NF-kB), activator protein-1 (AP-1), and signal transducer and activator of transcription-3 (STAT-3) (Kumar Rajendran et al., 2019). The activation of these transcription factors can have far-reaching effects on gene expression and cellular physiology (Fig. 2). NF-kB, in particular, plays a critical role in regulating various aspects of immune function, including the innate and adaptive immune responses, apoptosis, cell proliferation, and differentiation. Indeed, NF-kB has been shown to regulate the expression of numerous genes involved in key biological processes such as inflammation, angiogenesis, and stress response (Khalid et al., 2022). Impairment of NF-kB production or activation has been implicated in the pathogenesis of a wide range of diseases, including cancer, autoimmune disorders, inflammation, and viral infections. In addition to its role in regulating immune function, NF-kB has also been shown to play a crucial role in the regulation of cell survival and proliferation. Dysregulation of NF-kB activity has been linked to the development and progression of various human cancers, as well as other pathological conditions such as neurodegenerative disorders (Wasim et al., 2022).

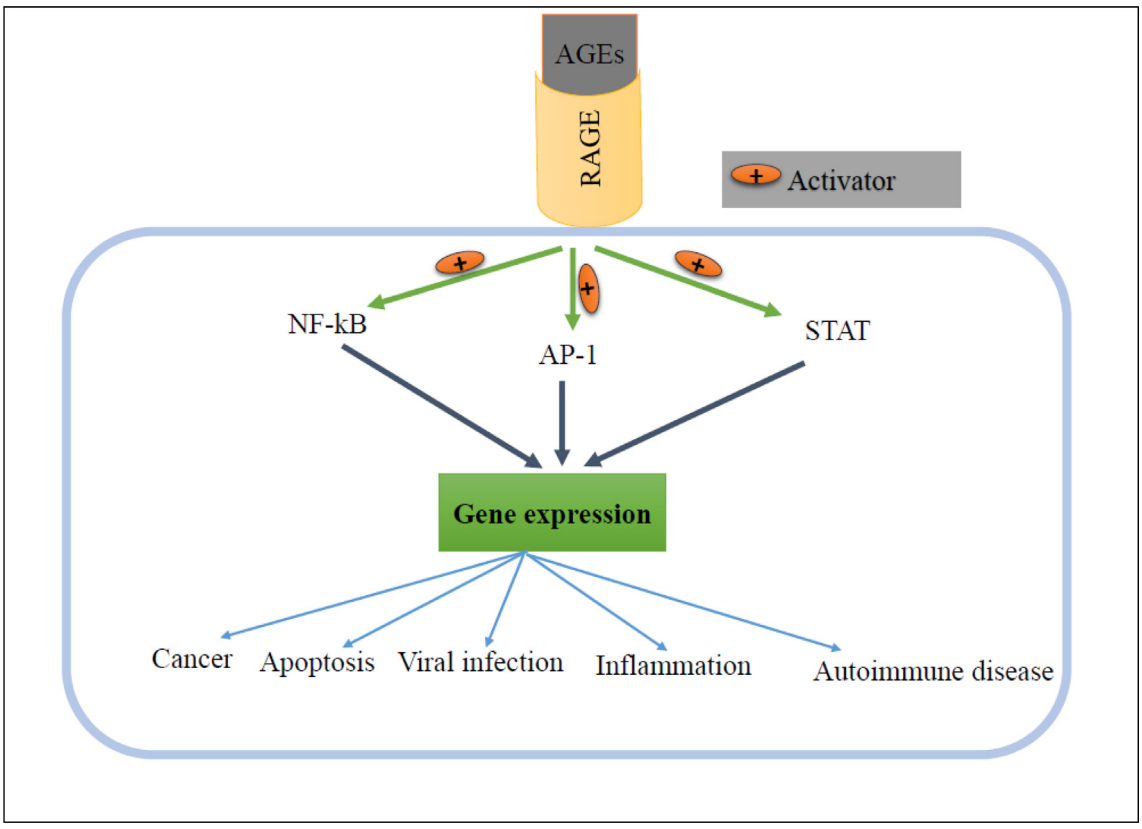

Fig. 2 Activation of factors related to gene expression and their effects due to AGEs bind to RAGEs.

The AP-1 and STAT-3 transcription factors are also implicated in a range of biological processes, including cell growth, differentiation, inflammation, and apoptosis. The dysregulation of these factors has been associated with a range of diseases, including cancer, autoimmune disorders, and inflammatory disorders. Overall, the activation of transcription factors by AGE-RAGE interactions has significant implications for cellular physiology and disease pathogenesis. Further investigation into the underlying mechanisms governing these interactions may yield promising therapeutic targets for a variety of human diseases (Rojas et al., 2013).

1.8. Exploring mechanisms for the prevention of AGEs

AGEs are known to play a critical role in the development of various physiological and pathophysiological processes. Consequently, inhibiting their formation and accumulation has emerged as a promising therapeutic strategy for preventing complications associated with diabetes and other chronic diseases (Singh et al., 2001). One crucial approach toward limiting AGE formation involves the activation of the body's natural defense systems. These systems involve a broad range of enzymatic and non-enzymatic processes that can prevent or reduce the production of AGEs. For instance, the enzyme glyoxalase I plays a critical role in detoxifying reactive dicarbonyl compounds, which are precursors to AGE formation. Similarly, antioxidant enzymes such as catalase and superoxide dismutase (SOD) work to scavenge ROS, which are known to promote AGE formation through oxidative stress (Fig. 3).

Glyoxalase I is an essential component of the glyoxalase system that plays a critical role in mitigating the detrimental effects of toxic metabolites, such as MGO, present in the cytosolic milieu of cells. It accomplishes this task by catalyzing the isomerization of MGO, consequently facilitating the spontaneous conversion of glutathione (GSH) to D-lactoylglotathione (Laus et al., 2023). This metabolic transformation effectively abrogates the production of harmful α-oxoaldehydes and AGEs that are implicated in various pathophysiological processes within the human body (Fig. 4).

1.9. Effect of synthetic and natural compounds on the AGEs formation

The primary mechanisms responsible for impeding the formation of AGEs involve curtailing the presence of active dicarbonyl compounds, degrading preexisting AGE compounds, safeguarding the structural integrity of proteins, and preventing reactive oxygen species (ROS) production. Several synthetic pharmaceutical agents have demonstrated efficacy in inhibiting AGE generation. Notably, aminoguanidine, the first clinically viable drug in this regard, operates by sequestering the carbonyl functional group of amadori products via nucleophilic addition reactions, which restricts the further rearrangement of these compounds. Additionally, aminoguanidine has been found to bind effectively with active α-dicarbonyl intermediates resulting in the formation of triazines, thereby blocking the conversion of Amadori products to AGEs. Despite its clinical usefulness, aminoguanidine's therapeutic value is limited due to prominent side effects that include the promotion of oxidation, vasculitis, lupus, gastrointestinal symptoms, and pernicious anemia (Schalkwijk and Miyata 2012). In the domain of pharmacology, compounds known as synthetic AGE breakers, specifically desferrioxamine, ALT-711, losartan, pyridoxamine, and clioquinol, have been demonstrated to facilitate the removal of carbon–carbon bonds between carbonyl groups, leading to effective elimination of cross-linked products (Table 2). Furthermore, certain hypoglycemic drugs like aspirin and metformin can impede the formation of AGEs (Luevano-Contreras and Chapman-Novakofski 2010). However, all of these aforementioned compounds are inevitably associated with undesirable reactions

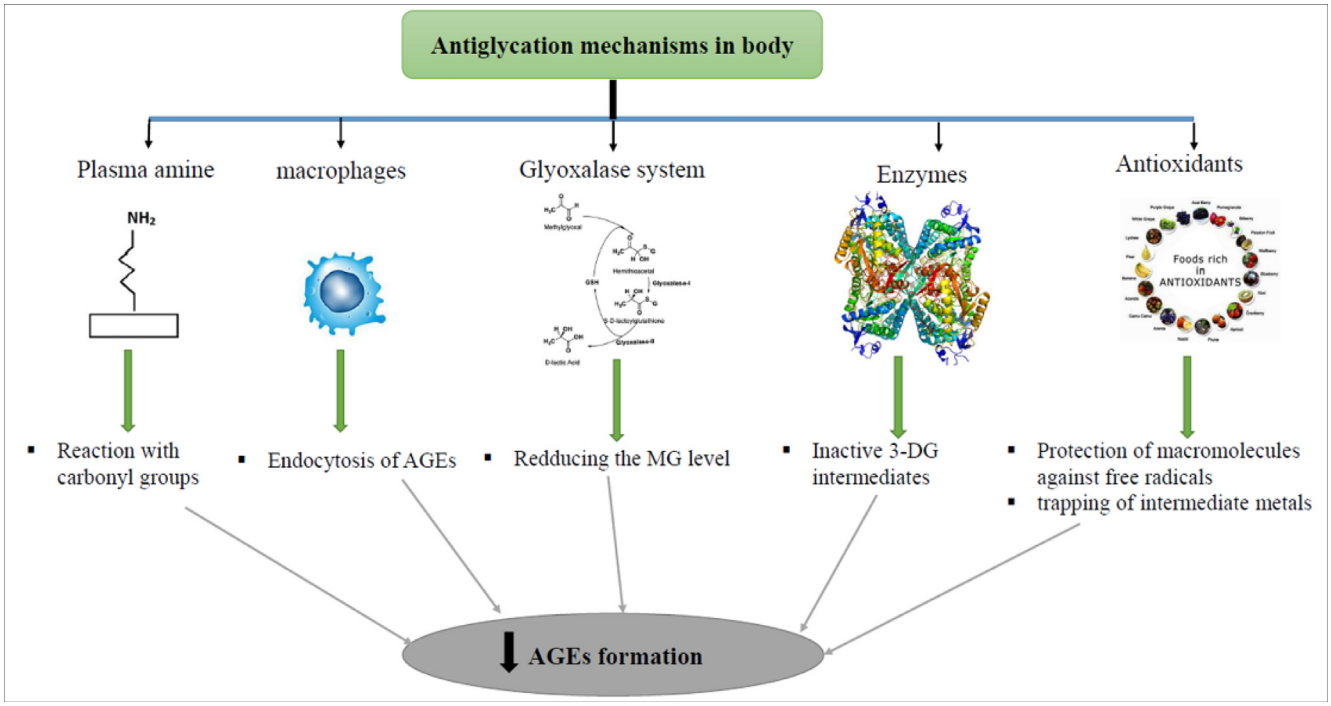

Fig. 3 A number of the body's defense mechanisms along with their function against AGEs (Abbreviation; MG, Methylglyoxal).

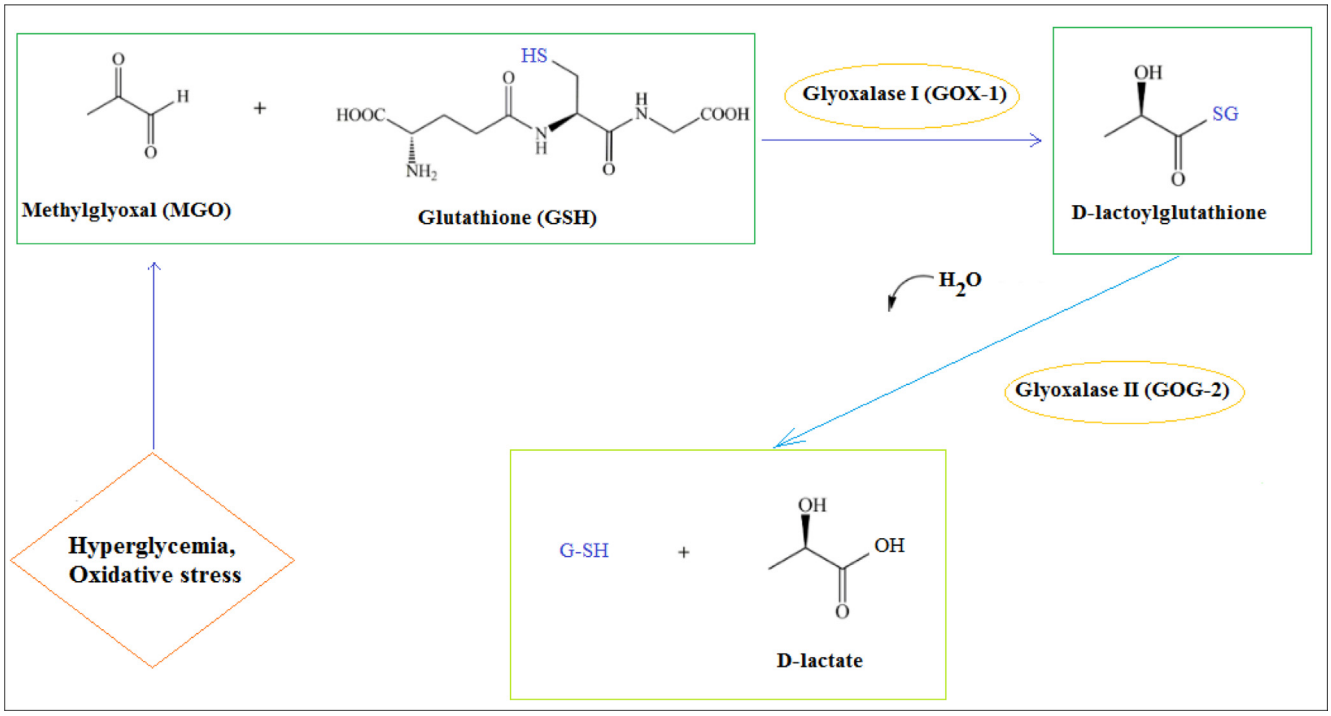

Fig. 4 The transformation of methylglyoxal into D-lactic acid is accomplished through the complex glyoxalases system, which operates in a GSH-dependent manner and entails a two-enzyme pathway featuring Glyoxalase I and Glyoxalase II enzymes. Specifically, Glyoxalase I serves as a catalyst for the formation of D-lactoylglutathione by facilitating the reaction between methylglyoxal and GSH. Subsequently, Glyoxalase II drives the hydrolysis of D-lactoylglutathione, leading to the production of D-lactic acid and GSH.

Table 2 A number of chemical antiglycations as well as their function.

Synthetic compounds	Antiglycation functional	Ref.
Metformin	Undergoes a chemical reaction with MGO resulting in the creation of the corresponding dihydroimidazolone derivative.	(Ahmad et al., 2013)
Aminoguanidine	The sequestration of reactive carbonyl moieties, including 3-dG, GO, and MGO, can be achieved through the formation of non-toxic adducts utilizing 1,2,4-triazines.	(Aminjafari et al., 2016)
Aspirin	acetylation of free amino groups	(Ahmad and Ahmed 2006)
Desferrioxamine	The inhibition of AGEs is attributed to their ability to chelate metal ions.	(Rai et al., 2021)
Losartan	Decreased serum AGEs	(Singh et al., 2001)
Clioquinol	The process of glycoxidation is impeded.	(Wu et al., 2021)
Pyridoxamine	Inhibitor of the change of amadori product to AGEs	(Adrover et al., 2008)
ALT-711	The covalent intermolecular bonds of pre-existing AGEs are impeded.	(Chen et al., 2020)
Thiazolidine Derivative	Prevent the accumulation of AGEs in the renal glomeruli	(Singh et al., 2001)

Table 3 A number of natural antiglycations as well as their function.

Natural compounds	Antiglycation functional	Ref.
Quercetin	Trapping of MGO and GO	(Li et al., 2014)
Lignan	Suppression of NADPH & ROS	(Kong et al., 2015)
Chlorogenic acid	Neutralize the effect of AGEs aggregation	(Zhao et al., 2022)
Curcumin	Elicits a reduction in the accumulation of collagen moieties that have undergone post-translational modifications via AGEs	(Alizadeh and Kheirouri 2019)
Resveratrol	Suppression of MG	(Ciddi and Dodda 2014)
α-Tocopherol	Demonstrates suppressive properties with respect to the formation of AGEs in experimental animal	
Hesperitin + Stilben	Block RAGEs	(Li et al., 2012)
Luteolin	Inhibitory effects on the early and middle stages of the glycation process	(Sarmah et al., 2020)

and lack long-term viability in clinical applications. Consequently, a more promising avenue of research involves exploring the safety and efficacy of natural compounds that can suppress AGE formation while exhibiting favorable activity and safety profiles.

The term "natural compounds" refers to chemical entities that are derived from botanical or zoological sources and exhibit distinctive pharmacological properties. The manifold benefits of natural compounds in terms of their biological activities are pervasive, encompassing a wide range of anti-inflammatory and antioxidant effects, as well as the inhibition of digestive enzymes such as α-amylase and α-glucosidase (Sadeghi et al., 2022, Sadeghi et al., 2022, Sadeghi et al., 2022, Fatullayeva et al., 2023, Gök et al., 2023). Furthermore, these compounds have demonstrated potent anti-apoptotic activity that holds great potential for therapeutic intervention (Pandey and Rizvi 2009). Additionally, they exhibit antiglycation activity by virtue of their ability to impede the formation of AGEs, thus conferring significant health benefits (Xiao and Hogger 2015).Currently, a number of natural compounds such as quercetin, lignan, chlorogenic acid, curcumin, resveratrol, α-tocopherol, and luteolin possess notable antioxidant characteristics, demonstrating potent inhibitory effects against the formation of AGEs with negligible toxicity (Luo et al., 2022). This compounds all possess potent anti-glycation properties due to their ability to scavenge ROS and inhibit advanced oxidation protein products (AOPPs) (Table 3). Consequently, the exploration of novel glycation inhibitors among natural compounds has emerged as a prominent research field in recent times, garnering considerable interest and attention.

2. Conclusion

Currently, extracting natural medicines and determining their molecular structure is considered as an inevitable path to start drug discovery. Several studies have shown that various natural compounds, such as quercetin, lignan, curcumin, resveratrol and α-tocopherol, are promising candidates for discovering new paths in inhibiting the formation of AGEs. These compounds interfere with the formation of AGE adducts by blocking protein glycation sites, scavenging active carbonyl compounds, regulating blood glucose levels, chelating metal ions, and removing free radicals. While the potential of natural compounds to serve as pharmaceutical agents is obvious, their bioavailability in clinical medicine is limited by the first-pass effect, which reduces their concentration through oxidation and gly-oxidation. Therefore, understanding the mechanisms of action of natural medicines provide a convenient platform for the development of new AGE-suppressor-

drugs discovery. Nevertheless, the identification of new drugs among natural compounds warrants more attention, as safety and efficacy issues must be carefully considered.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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