Anti-Cataract and Plant Extracts-Based Natural Products: A Review

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ABSTRACT
Cataracts are of concern to the world as one of the diseases that cause blindness. Diabetes mellitus has a relationship with cataracts due to hyperglycemia through polyol pathways that are converted to sorbitol by the aldose reductase enzyme. Polyol pathway has implications for the pathogenesis of the formation of diabetic cataracts. The use of anti-cataract drugs using plants is considered as a solution for the formation of diabetic cataracts. Several studies on plant material have been developed for the treatment of diabetic cataracts that assess the performance potential of bioactive compounds through inhibition of the enzyme Aldose Reductase. Studies from various recent research results provide information that plants as natural products have the potential for a large solution of diabetes cataract prevention and treatment.

Keywords: Cataract, Hyperglycemia, Plants extract, Polyol Pathway, Aldose Reductase Inhibitor
1. INTRODUCTION
Cataracts in Asia like China, India, Taiwan and Singapore averagely has prevalence of 14% to 49%, where in the future the trend of cataract associated visual impairment is increasing [1]. Visual impairment is a serious problem in the whole world, in fact blindness, as one of visual impairments, has become global issue with the percentage of more than 1% of the total world population. World Health Organization (WHO) reported that the distribution of world population blindness has reached 45 people, especially in developing country such as Indonesia [2, 3]. A survey in 39 countries around the world reported that out of 285 people who have visual impairment, 50% of which is attributable to cataract affected by the age, diabetes complications and 13.7% blindness [4].

In some cases, free radicals trigger to induce lens opacification. The modification of protein by free radicals has been linked to severe oxidative stress, and some studies shows that natural products from plants could be prevented protein insolubilization thereby delaying lens opacity [5].

Natural compounds consisting of antioxidant or anti-inflammatory secondary metabolites can serve as potential leads for anticataract agents. In this review, we tried to gather information form evidence plant-based natural products used for cataract treatment. This literature review is aimed at the evaluation of the potential natural products for anti-cataract.

Cataract and Diabetes Mellitus
Increasing trend of cataract sufferer follows the complications development of diabetes mellitus. Diabetes mellitus (DM) is an non-infectious disease with the characteristics of hyperglycemia [5]. It is associated with the organ pathophysiology caused by the dysregulation of metabolism of the sufferer, in which it can further cause various health complications [6] such as eyes impairment (retinopathy, cataract, etc.) as well as another organs impairment. Diabetes is one of the major causes of cataract development.

The increase of blood sugar concentration in diabetes is a significant cause of the diabetes complications that is cataract, where during hyperglycemia, glucose is converted through polyol pathway into sorbitol by aldose reductase enzyme, then into fructose with the sorbitol dehydrogenase acts as the catalyst [7]. Since polyol pathway has pathogenesis implication against diabetic cataract, it is suggested to do a prevention by inhibiting the enzymatic activities [8-10]. Aldose reductase (AR) is the main enzyme and the regulator in polyol pathway, where it catalyzes the formation of sorbitol by reducing the glucose aldehyde formation through NADPH conversion into NADP+ simultaneously [11]. Consequently, tissue oxidative stress experiences an increase due to the depletion of NADPH activating the polyol pathway. In hyperglycemic condition of polyol pathway, there would be a different glucose metabolism compared to the normal condition. This difference allows the sorbitol-induced osmotic stress damaging the lens fibril and causing cataract, where the it is also possible to generate the oxidative stress causing other diabetic complications [12].

Glucose toxicity has a significant contribution against the development of eye complications of diabetes sufferers [13]. By focusing on aldose reductase inhibition, the diabetic complications can be reduced. Studies on aldose reductase inhibitor molecules through plant sourced synthesis is carried on in various laboratory experiment, even though a lot of improvement is needed, especially in safety and effectiveness of the synthesized product aspects [14, 15]. Many animal tests such as on mice, goat and rabbit, have been conducted to develop a safe and effective aldose reductase inhibitor, where its availability can meet the current market demand.

Diabetic Cataract Treatment
Until recently, surgery is the only treatment to remove cataract [16]. This adds more extraordinary socio-economic burden, especially in rural areas, where diabetes treatment and cataract surgery often neglected. Nevertheless, several revolutionary studies on non-surgery cataract treatment has been conducted to answer the world’s blindness problem [17].

However, the effectiveness of this medication treatment does not have sufficient scientific proof, such as the experimental use of sorbitol concentration reducing drug on animals, where the it inhibits the glucose conversion into sorbitol, showed a positive result of diabetic cataract [18-20]. The application of anti-cataract drugs is considered as an alternative to reduce the effect of risking factors by controlling the
blood glucose and consuming anti-oxidant rich nutrients [21].

**Anti-Cataract and Natural Plants**

The application of plants as traditional medicine has been practiced for more than thousands of years [22]. Development of scientific knowledge has motivated the studies to search the plant potentials as herbal medicine. It contains bioactive components such as flavonoid, this component represents phenolic compounds which can be widely found in various plants, where it also possesses useful health attribute for humans. That includes the anti-oxidant activity which protect the body from free radicals and other activities such as anti-bacteria, anti-microbe, anti-mutagenic and anti-inflammatory. The compounds ability to inhibit enzymatic activity has also been reported [23].

Traditional medicines are sourced from plants that are rich of bio-compounds and have the chemical uniqueness, thus more biomaterial-based medicines keep developing [24]. New bioactive compounds of flavonoids are the future research objective, to obtain it from various plants and evaluate its active structure. Exploring the correlation between the compound structure and its bioactivity, is a strategic approach to discover an ideal herbal medicine [25, 26].

2. **DISCUSSION**

The trend of plant-based biomaterials exploration pertaining anti-diabetic cataract has shown to be a potential source of Aldose Reductase Inhibitor (ARI). Some of the products act as pharmacology agents that inhibit AR, in which they have low toxicity due to their original sources from plants and fruits [27-30]. Some of known plant extract bioproducts that possess ARI activity are *Ocimum sanctum*, *Withania somnifera*, *Curcuma longa* and *Azadirachta indica* and *Diabecon Indian* herbal [31, 32]. Recent studies within the last five years regarding the application of plant-based anti-cataract drugs can be observed on Table 1.

Besides, synthetic and semisynthetic product of ARI have also been developed with various types of medicine, but their effectiveness and side effects are still considered to have significant usage limitation. The medicine includes nonsteroidal anti-inflammatory drug such as Sulindac [33, 34], Aspirin [35, 36] or Naproxen [37], which have been reported to give an effect of cataract delay on diabetic rats through weak AR inhibition. Despite those results, it can still be concluded that ARI is effective against oxidative stress, thus preventing the development diabetes-induced cataract.

| Table 1. Plant extracts that have effectiveness and activities of AR inhibition [40-48] |
|---|---|---|
| No | Extract | Activity |
| 1 | Methanolic extract of *Punica granatum* leaves | Anti-diabetic activity, AR inhibitory activity and anti-cataract activity in vitro in goat lenses |
| 2 | *Dendrobium aurantiacum* var. *denneanu* | The effect of Gigantol on the development and progression of galactose induced cataract, inhibit enzymatic activity of the AR and iNOS in vitro and in vivo in rat lenses |
| 3 | Ethyl acetate fraction of *Saraca indica* (SI) | Aldose reductase (AR) inhibitory activity and anti-cataract activity in vitro in rat lens |
| 4 | *Zea mays* L. (purple waxy corn) seeds extract | Aldose reductase activity, oxidative stress plays activity (Superoxide Dismutase, Catalase, Glutathione Peroxidase) in vitro in Male Wistar rats lens |
| 5 | Ethanolic extract of seed kernel of *Caesalpina bonduc* a (L.) Fleming | Anticataract activity in vitro in Goat lens |
| 6 | Methanol extract and water extracts of *Coccinia* | Antioxidant activities and aldose reductase inhibitory activity - |
**grandis** (L.) fruits (CGFs)

7 Flavonoids active components of *Vernonia cinereal* (lupeol)

Antioxidants activities in *In vivo* cataract rats

8 Fruit, Pericarp and seeds of 80% ethanol extract from *Cornus officinalis*

Inhibitory effect on AGE formation, Rat Lense Aldose Reductase Activity, Collagen AGE cross linking, Xylose-induced catactogenesis, and breaking action on AGE-protein cross links in *In vitro* lens Rats

9 Ethanol extract from *Chromolaena odorata* leaves

Antidiabetic activity with prevention of cataract formation in *In vitro* diabetic rats

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Several laboratory tests on animals such as mice, goat and rabbit have been massively conducted, where it is expected that the ARI activity can be safe, effective and available for market demand. The experimental researches are more intense by employing plant-based biomaterials, where they have shown a significant role in AR inhabitation, especially when these materials do not only delay the cataract formation but also the preventing the cataract itself.

Researches on rats have been carried out to evaluate the inhibition ability of the biomaterials against AR enzymatic activity, obtained from *Punica granatum* leaves [40], *Dendrobium aurantiacum var. denneanumis* [41], *Saraca indica* [42], *Zea mays* leaves [43] and *Chromolaena odorata* leaves [48]. Additionally, some fruits have been studied to have the similar AR activity such as *Cornus officinalis* [47]. The activity of these plant extracts, do only possess the ability to inhibit AR, but also give other effects, which contribute to the in vitro and in vivo experimental results.

3. CONCLUSION

A review of those articles gives an information that plant as biomaterial resources, have a big potential in preventing and curing diabetic cataract. The researches offer a portrayal of plant-based biomaterials development as anti-cataract drugs, where other strong activities are also have been reported, such as anti-oxidant, AGE formation inhibition, anti-cataractogenesis and anti-diabetic.

REFERENCES


