ANTIOXIDANT AND ANTIDIABETIC ACTIVITY OF ETHYL ACETIC EXTRACT ON EDIBLE MARINE ALGAE (*Halymenia durvilae*) COLLECTED FROM NORTH SULAWESI COASTAL AREA OF INDONESIA

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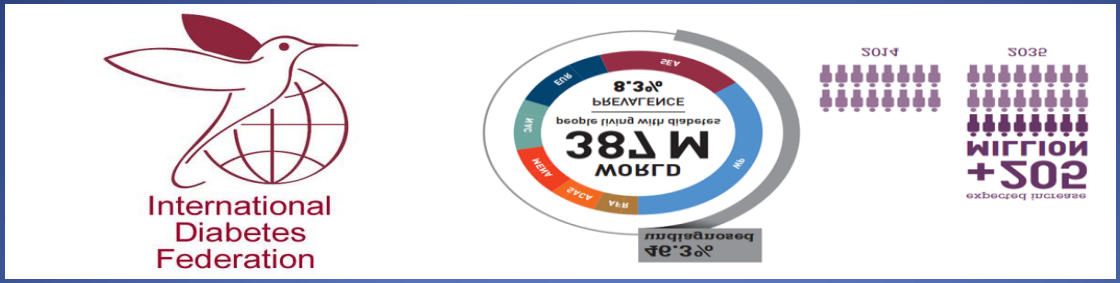
Introduction



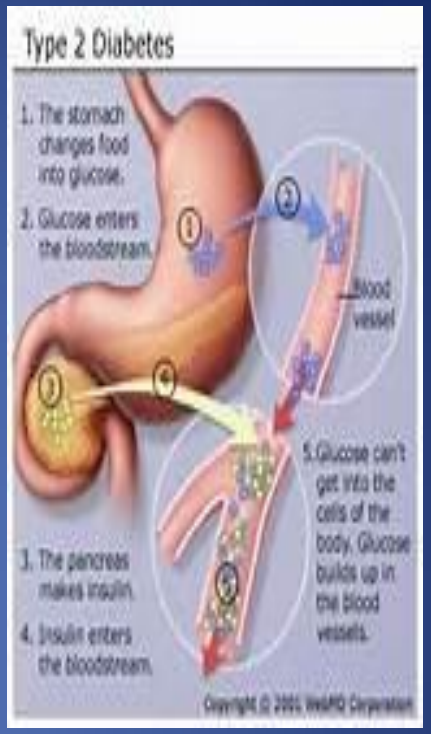
The incidence of diabetes is increasingly at an alarm rate due to changes in modern lifestyles. The International Diabetes Federation estimates that 387 million people live with diabetes around the world in 2014 and that number is estimated to grow to nearly 600 million by 2035.

There were 9.1 million cases of diabetes in Indonesia in 2014. It also has the fifth largest number of diabetic patients. According to WHO data, the prevalence of type 2 diabetes mellitus (T2 DM) in Indonesia will be increasing 14.1 million in year 2035. (Cho, 2014).

The recent approach for controlling postprandial hyperglycemia is to inhibit the carbohydrate hydrolyzing enzymes such as α-amylase dan α-glucosidase in the digestive system. The commercially avaluable synthetic antidiabetic drug include Voglibose and miglitol,

However many of these synthetic hyperglycemic agents have their own limitation. They are non-specific, produce serious side effects and fail to reduce the diabetic complication. They often cause severe gastrointestinal side effects (Shimabukuro *et al.,* 2009).

-Numerous natural products such as crude extracts and isolated compounds from seaweeds appear to be applicable as antioxidant and anti-diabetes.

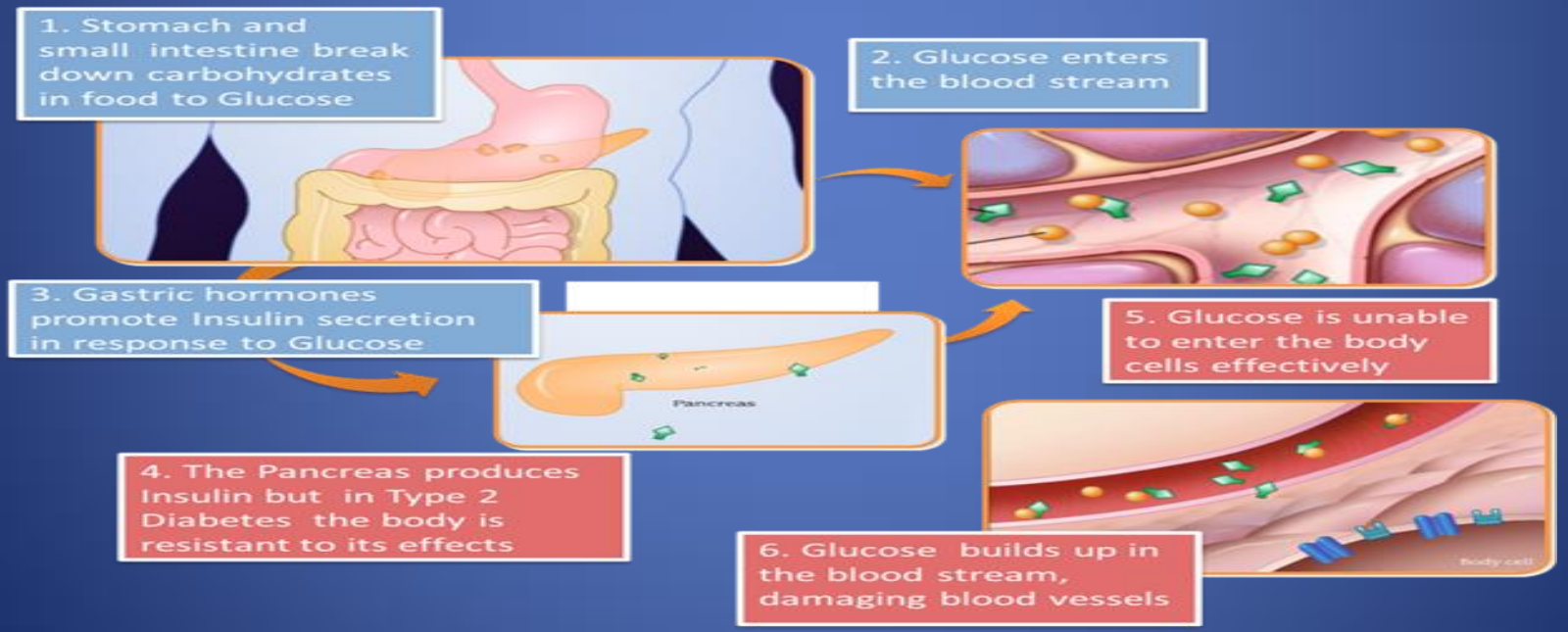


Due to the potentially harmful side effects related with antioxidant and anti-diabetes drugs as long-term treatments, showing of natural sources with reducing minimal side effects has drawn much attention.

Reactive species Oxygen (ROS) is generated in living organism during metabolism. It's produced in form of superoxide anion (O^{-2}), hydroxyl radical (•OH), peroxyl radical (ROO•), hydrogen peroxide (HOOH) and nitric oxide radical (NO). ROS damage biological molecules for instant lipids, protein, enzymes, DNA and RNA leading to cell or tissue injury, plays a role in a broad general disease and age-related to degenerative condition.

These consist of cancer, diabetes, stroke, inflammatory condition and neurodegerative diseases, On the other hand, antioxidant is believed to be defensive because it may help to shelter the human body against damage by ROS.

Diabetes mellitus is a group of chronic diseases, which can be recognized to hyperglycaemia, a situation characterised by an extreme concentration of glucose circulating in the blood, with unsteadness in carbohydrate, fat and protein methabolism.

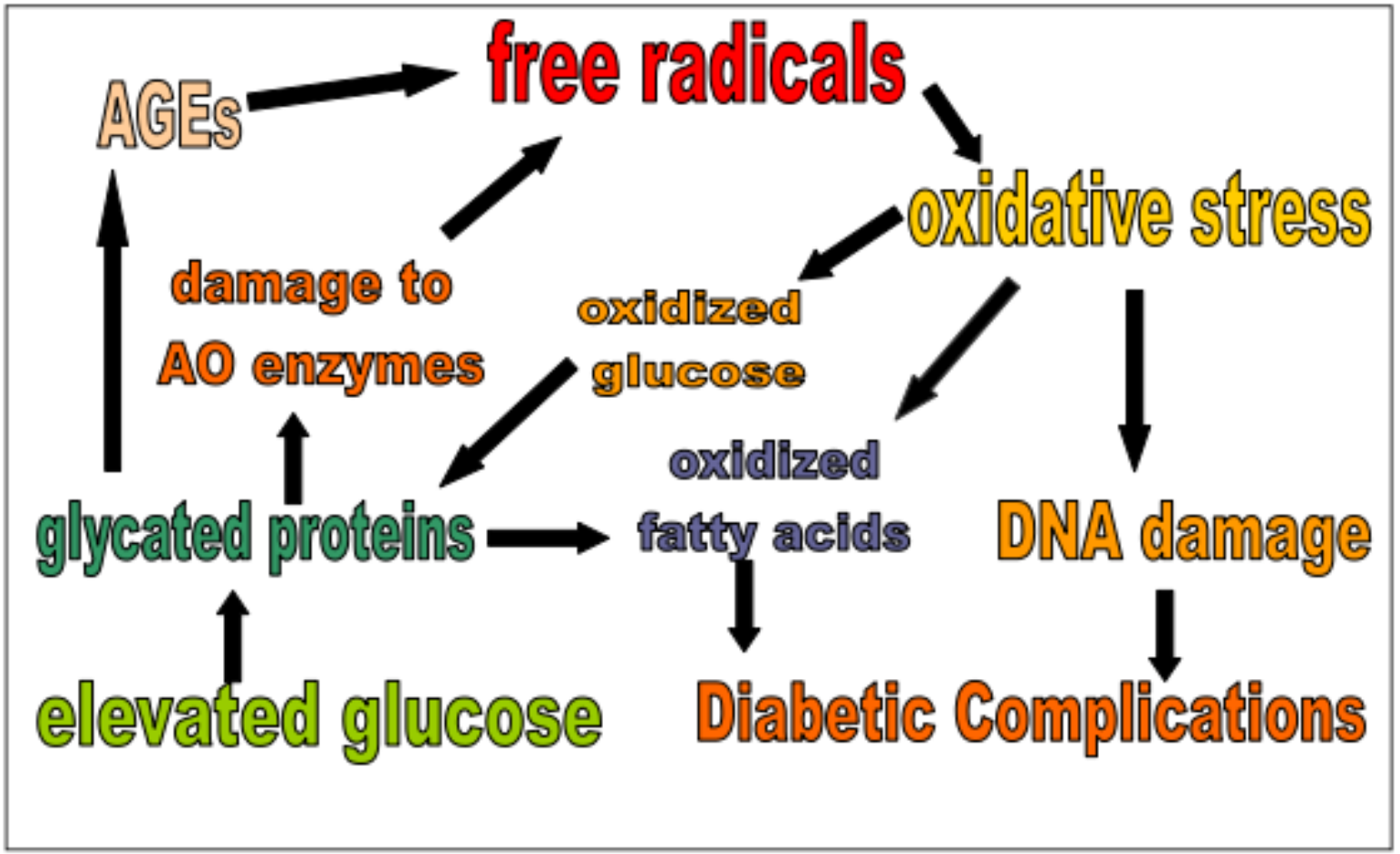


Diabetes mellitus can be categorised into two main forms namely:

- Type I diabetes mellitus (T1DM), caused by the absolute nonattendance of insulin production due to auto-immune mediated colapse of pancreatic β-cells, and
- Type II diabetes mellitus (T2DM), which is due to the virtual insuficiency of the same hormone concerning insulin resistance, percullar synthesis of hepatic glucose and progressive deterioration of pancreatic β-cell functions

What Causes Diabetes? A number of lifestyle factors are known to contribute to the development of Type 2 Diabetes. Excess weight, defined as a body mass index (BMI) of 25 or more, leading an inactive lifestyle, having abnormal cholesterol and blood lipids, high blood-pressure and smoking are all factors that increase the risk of developing Type 2 Diabetes.

Oxidative Stress and Diabetic Pathology



Seaweeds have been suggested as a promising source of bioactive substance that might have pharmacheutical Aplication (Nousu *et al*., 2011). It's source of dietary fiber especially soluble fiber such as alginates which can influence satiety and glucose intake from food.

- Natural products and their derivatives represent more than 50% of all the drugs in clinical use of the world are known to possess antioxidant potential. Thus, potential antioxidant and antidiabetic properties of plant extracts or isolated products of plant origin can possibly be explored for developing the antidiabetic drugs (Boopathy and Kathyresan, 2010)

The objective of this research was to evaluate:

1. Total phenolic content
2. the antioxidant activity (DPPH, FRAP assay and FIC assay.
3. I*n vitro* α-glucosidase inhibitory activity of ethyl acetic fraction of *Halimenia durvilae* collected from North Sulawesi coastal area of Indonesia.

2. Metodology

- Freeze fresh sample of seaweeds extracted using 70% methanol (1/2, w/v) The extract obtained was fractionated using ethyl acetic.
- The extract and fractions storage at -20℃ for future analysis.

Chemicals and reagents

- 1,1-diphenyl-2-picrylhydrazyl (DPPH) was purchased from Sigma Aldrich, Ferozin iron reagent, Follin-Ciocalteu's phenol, sodium carbonate (Na_2CO_3), methanol, potassium dihydrogen phosphate (KH_2PO_4, iron (III) chloride-6-hydrate ($FeCl_3$), Trichloroacetic acid (TCA) and Potasium ferricyanide $K_3Fe(Cn)6$ purchased from Merk Spanyol.
- α-glukosidase, ρ-nitrophenil-α-D-glucopyranoside, phosphate buffer, sodium carbonat were purchased from Sigma-Aldrich (St. Loius, MO. USA.) All other solvent and Chemical were analytical grade.

3. Result and Discussion

Tabel 1. TPC, FRAP, FIC and DPPH of *H.durvilae*

Parameter	Value
TPC	11.55± 7.50 mg GAE/100 g
FRAP	35.27± 0.93 uM Fe^{2+} mg^{-1} extract.
FIC (IC_{50})	31.52 ± 2,903 mg/ml
DPPH (IC_{50})	11.95 ± 0.34 mg/ml
BHT(IC_{50})	0.1467 mg/mL

Antidiabetic Activity

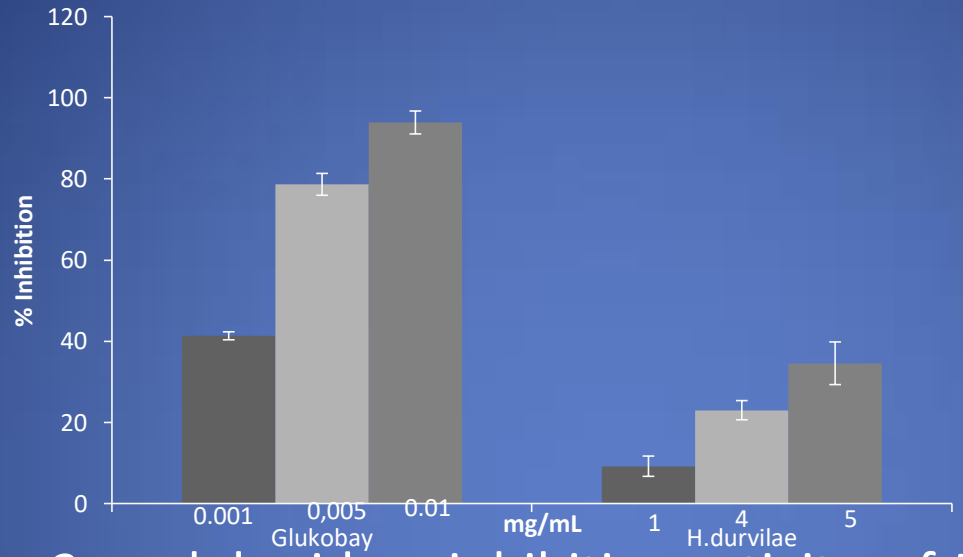


Fig. 2. α-glukosidase inhibition activity of *H.durvilae*

- The α-glucosidase inhibition effectiveness of extracts were compared on the basis of their % inhibition (IC_{50} 8.05±0.43 mg/ml) and the control positif of glucobay was IC_{50} 0.0011 mg/mL

The extract and its fraction were found to possess α-glucosidase inhibitory effect on starch break down *in vitro*. The α-glucosidase effectiveness of extract and fraction were compared on the basis of their % inhibition (1-5 mg/ml).

Many natural resources heve been reported for their antioxidant and antidiabetic activities for treatment of diabetes. Polyphenols from edible seaweeds have also been suggested to influence responses relevans to diabetes trough modulation of glucose induced oxidative stress, as well as through inhibition of starch-digestive enzymes (lee *et al*., 2010).

- Red seaweeds of the family Rhodomelaceae contains bromephenols with α-glucosidase activity; one of the family Rhodomelaceae bears a 3,4- dihydroxybenzyl skeleton (Senthil *et al.,* 2013). Kim *et al.,* 2009 reported the α-glukosidase and α-amilase inhibitor bromephenol C_6H_5BrO is produced by red algae *Polyopes lancifolia* and *Grateloupia elliptica* without toxic effect.

- Diabetic complications may also be explained by increases in DNA damage due to oxidative stress. DNA damage was measured in 10 normal and 10 diabetic patients. A significant elevation in DNA strand breaks and oxidized pyrimidines was seen in patients with Type I diabetes compared with normal subjects. Altered purines showed a strong positive correlation with blood glucose level (Collins et al. 1998).

- Glycation of proteins leading to the accumulation of advanced glycation end products (AGEs) is known to be one of the sources of free radicals and has been strongly linked to the presence of diabetic complications (McCance et al. 1993). These glycation products may directly release superoxide radical and H2O2, activate phagocytes, and reduce glutathione levels (Gutteridge and Halliwell, 1999)

4. **CONCLUTION**

- This study is a priliminary report on-antidiabetic properties of seaweeds *H. durvilae.* The *in vitro* α-glucosidase activity of ethyl acetic showed good result, in inhibition of diabetic. Therefore edible seaweed *H.durvilae* could be used as dietary food source of natural antidiabetic agent. In future isolation of ethyl acetic extract of H. durvilae need be performed to know the bioactive compound that function as antidiabetic.

Thank you