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REVIEW ON: NATURAL DRUG (BIOFLAVONOID) USE IN TYPE-2 DIABETES MELLITUS: BIOFLAVONOID SHOW A GOOD ANTI-DIABETES PROPERTIES

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ABSTRACT-

This review explores the role and effectiveness of bioflavonoids in the management of Type-2 Diabetes Mellitus (T2DM). Diabetes Mellitus is characterized as a chronic metabolic disorder resulting from defects in insulin secretion, insulin action, or both, leading to hyperglycemia1. While Type-1 diabetes is rare, Type-2 DM accounts for approximately 95% of all cases and is primarily driven by insulin resistance, where body cells fail to respond properly to the hormone. Bioflavonoids (or flavonoids) are natural polyphenolic compounds widely distributed in the human diet, found in sources such as citrus fruits, tea, vegetables, and dark chocolate4.... Structurally, they possess a 15-carbon skeleton (C6-C3-C6) and are classified into three main groups: bioflavonoids, isoflavonoids, and neoflavonoids4. Research indicates that these compounds exhibit a broad range of biological activities, including antioxidant, anti-inflammatory, and anti-diabetic properties. Specifically, bioflavonoids like Hesperidin show significant promise as anti-diabetic agents by modulating oxidative stress and inflammation. Given their low toxicity compared to other active plant compounds and their widespread availability, bioflavonoids represent a viable natural therapeutic strategy to improve the quality of life for the growing global diabetic population.

Keywords: Diabetic, Antioxidant, Anti-Inflammatory, 2 Diabetes Mellitus, Bioflavonoids

INTRODUCTION –

Diabetes Mellitus (DM): Diabetes mellitus is a disorder or condition in which defects in insulin secretion, insulin action, or both [1]. On the other hand diabetes mellitus is a chronic disease in which the pancreas disease does not produce sufficient insulin or when the body cell cannot effectively use the insulin it produces [2]. Insulin is a hormone produced by pancreas and regulates blood sugar levels, many types of symptoms are produced in diabetes mellitus patients like, high blood sugar, frequent urination, increased hunger, and increased thirst [2]. Diabetes mellitus are categorized in three types. [1]

1.	Type-1DM(Insulin-dependent diabetes mellitus)	In which pancreas cannot produce sufficient insulin, It mainly develops in childhood, and patients are taking lifelong insulin injection.
2.	Type-2DM(Non-insulin-dependent diabetes mellitus)	Specific body cells are responding to insulin hormones but in the case of TYPE2 DM these cells fail to respond to insulin properly. This type of diabetes is more common (about 95% diabetes cases are TYPE2-DM) [1]
3.	Gestational Diabetes(GDM)	This type of diabetes is diagnosed during pregnancy, It is a very rare type of diabetes, and its mechanism is not well understood. [1][2]

Note: type 1 diabetes mellitus (DM) cases is very rare about only 5% diabetes case is type 1 DM but, type 2 DM is very common, approx. 95% cases are type 2 DM , and mostly type2 DM patients are adults.[3]

Causes of diabetes mellitus:

Insufficient production of insulin, production of defective, or the inability of cells to use insulin properly and efficiently leads to hyperglycemia and diabetes. [4]

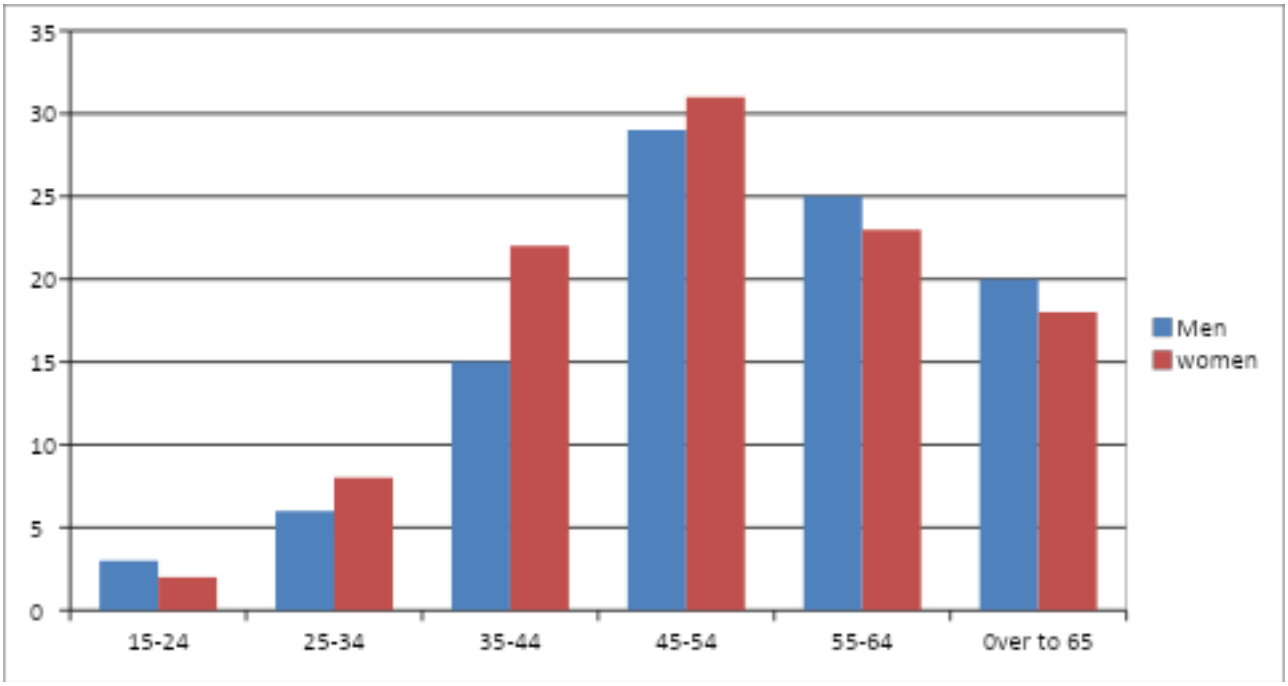
- This condition affects mostly the muscle cell and fat tissues, and results in a condition known as insulin resistance. This is the primary problem in type 2 diabetes. [4]
- The absolute lack of insulin, usually secondary to a destructive process affecting the insulin-producing beta cells in the pancreas, is the main disorder in type 1 diabetes. [4]

In type 2 diabetes, there also is affect the beta cells that adds to the process of elevated blood sugars. Mainly, if someone is resistant to insulin, the body can, to some degree, increase production of insulin and overcome the level of resistance. After time, if production decreases and insulin cannot be released as vigorously, hyperglycemia develops. [4]

Geographical data:

Kuwaiti:

Nabila A. Abdella and Moustafa M. Khogalib was perform a study in Kuwaiti in 1995 in this study,3299 Kuwaiti patients (1454 male (M) and 1845 female (F) subjects) registered in Salmiya diabetic clinic, a part of the national network of diabetes control and care programed and located in the urban Hawally Governorate, Kuwait, The age of the patients was 53 years (f 13.9 years), and 73.8% were in the age group 45-64 years. The majority of patients (53.6%) were diagnosed as they were clinically symptomatic in contrast significant minorities (37.8%) were diagnosed by chance mainly during investigation or unrelated events. The 8.6% of the women diagnosed during pregnancy had a high parity index 6.5 f 2.9. The actual duration of diabetes Mellitus was (7.8) years (range 2 -28 years) and 70% of the patients had diabetes mellitus for 9 years or less. The mean body mass index (BMI) was 31.8 f 6.3 kg/m2 and 28.5 f 6.3 kg/m2 in women and men, respectively. Among the Diabetic women 7.7% were obese (B M > 30 kg/m') and 30.2% were overweight (BMI 25-30 kg/m') as compared to 33.6% and 4 4.3% among diabetic men, respectively. High blood pressure (2160/95mm Hg) was reported in 14.9%. The main therapeutic modality in the majority of patients, (63.2%), was the administration of oral hypoglycemic agents (OHA), while 23.7% were on a diet regimen and only 13.1% were on insulin therapy. [5]



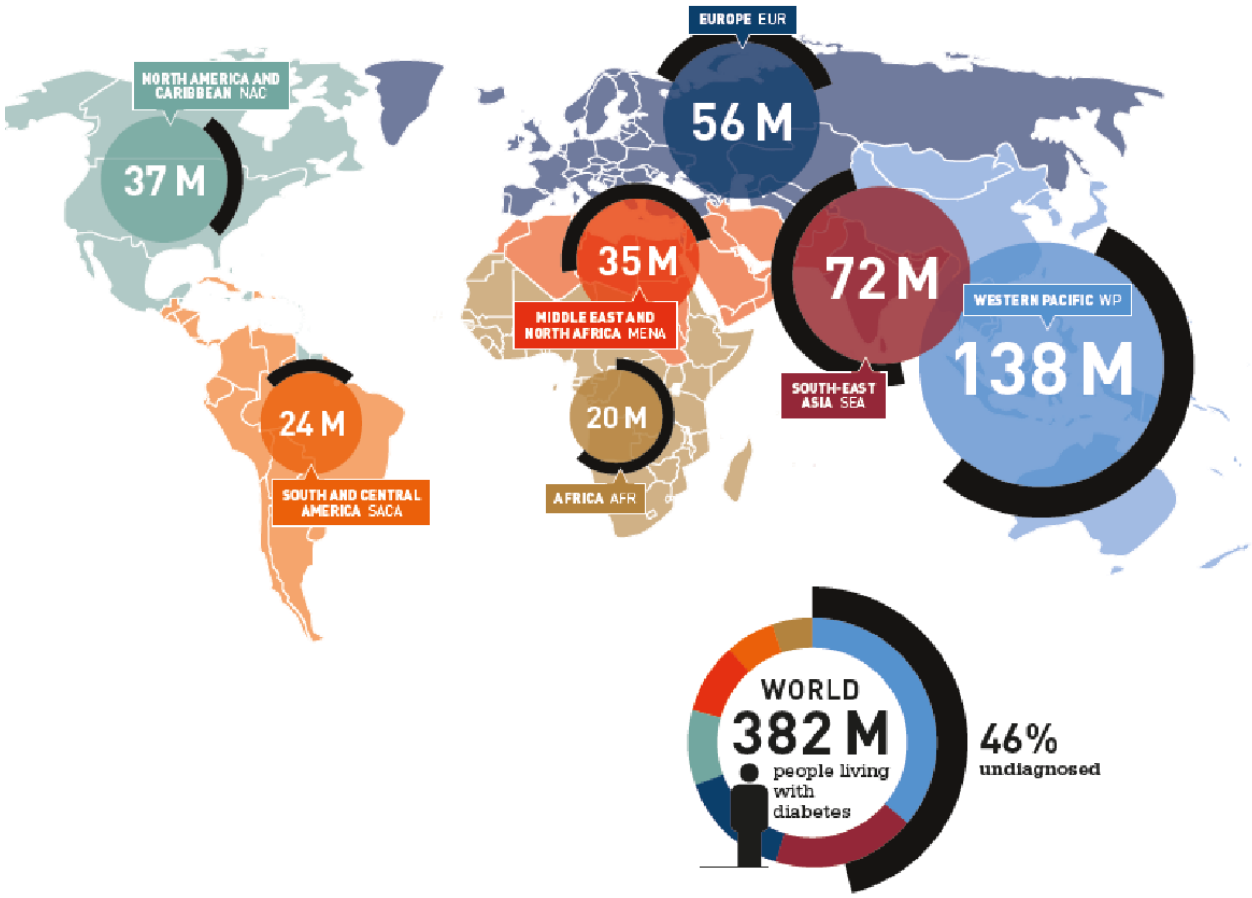
Age and sex distribution among 3299 Kuwaiti diabetic patients. [5]

Middle East:

A. Ramachandran, J-M. Chantelot, J. José Gagliardino surveyed the impact of diabetes education and self-management, in the Middle East [6]. According to this study about 1316 participants with T1DM (52% male) recruited by 762 investigators across Waves 2–4 in the *Middle East*, the age of participants was 32.4 (± 12.9) years, [6]. Overall, 59% of participants had received diabetes education. Overall, 75% of participants practiced SMBG (Self-management behaviors) but only 54% of participants practiced self-management. [6].

India:

According to a study (*Chhaya S. Chaudhry*), every day, In India about 5,000 new cases of diabetes are added. And its current diabetic population of 65 million people[7]. In this study 36 interviews were carried out between 24 April 2014 and 6 July 2014 over a period of 74 days. The study was done on 60 patients with foot sole pain, a condition caused by diabetes.[7] Top 10 countries with diabetic populations include both developing and developed nations, The most richest countries like- The United States, Japan, and Germany- also appear in the list of the top 10 nations with diabetic people, and highly populated countries such as China , India, and Indonesia.*The name of top 10 countries, and the number of people (20-79 year), which suffering from diabetes in this country 2013*- China(98.4M) , India(70.1M), USA(24.4M), Brazil(11.9M), Russian(10.9M), Mexico(8.7M), Indonesia(8.5M), Germany(7.6M), Egypt(7.5M), Japan(7.2M),[8]



Global incidence of diabetes. From *Global Diabetes Atlas* (6th edition.), by the International Diabetes Federation, 2013. Retrieved from http://www.idf.org/sites/default /files/ The_Global_Burden.pdf. [8]

Prevention of diabetes mellitus:

Diabetes management is to improve the quality of life and productivity of people living with diabetes. There are two methods of managing diabetes. (Diabetes education goes hand in hand with these two methods)

- Non drug method (use of proper diet and physical activity). -

-Use of Drugs e.g. diabetes tablets for lowering blood sugar and insulin.-

- Biguanides: *Metformin*,
- Sulfonylureas: *Glyclopyramide, Glibenclamide*
- Meglitinides: *Repaglinide*
- Thiazolidinediones: *Rosiglitazone*
- Alpha-glycosidase inhibitors: *Acarbose*
- Bioflavonoid: *Hesperidin*[9]

These are the same oral hypoglycemic agents, and most newly categories are bioflavonoids,

Bioflavonoid-

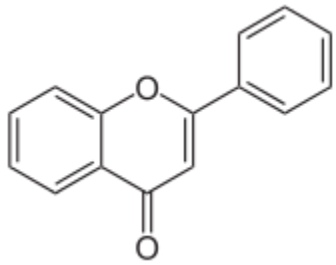
Bioflavonoids or Flavonoids, are made by the Latin word *flavus*, which means *yellow*, their color in nature. [10]. At structure level bioflavonoid contain (15-carbon skeleton), This skeleton contains two phenyl rings (A1 and B2) and a heterocyclic ring (C3). This model of carbon structure is also known as C6-C3-C6. According to the IUPAC nomenclature. [10][11].

Bioflavonoids are classified into mainly three classes: [12]

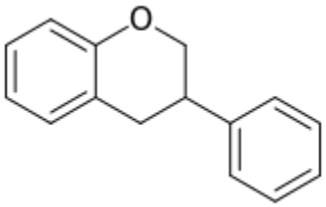
-*Bioflavonoids* or Flavonoid

-*Isoflavonoids*, derived from 3-phenylchromen-4-one (3-phenyl-1, 4-benzopyrone) structure

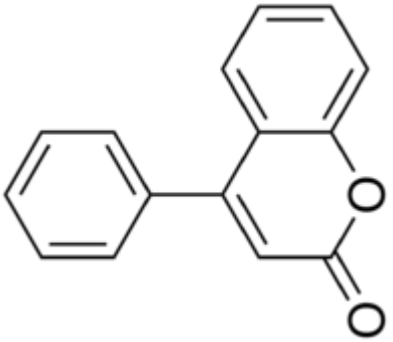
-*Neoflavonoids*, derived from 4-phenylcoumarine (4-phenyl-1, 2-benzopyrone) structure



Molecular structure of the flavone backbone (2-phenyl-1,4-benzopyrone)



Isoflavan structure



Neoflavonoids structure

Sources of Bioflavonoids-

Flavonoids are the mostly common group of polyphenolic compounds, which are present in the human diet and are found mainly in plants.[13] Flavonols, are original bioflavonoids (like-Quercetin), are also found in various plant, but in lesser amount. bioflavonoids widespread distribution and, they available in various variety and It produce low toxicity compared to other active plant compounds (like-alkaloids). High flavonoid contenting foods include- Parsley,[14] Onions,[14] Blueberries and other berries,[14] Black tea,[14] Green tea and Oolong tea,[14] Bananas, all Citrus fruits, Ginkgo biloba, Red wine, Sea-buckthorns, Buckwheat,[15] and Dark

chocolate (with a cocoa content of 70% or greater). According to the US Department of Agriculture flavonoid database.[14] These are the same Dietary sources of flavonoid.

Dietary intake Data-

United States Department of Agriculture (USDA), provide food commotion data for flavonoid. [16] In United States, According to NHANES "The National Health and Nutrition Examination Survey", about 190 mg/d flavonoid used adults, with flavan-3-ols as the main contributor. [17]. (NHANES is a survey research program conducted by the National Center for Health Statistics (NCHS) to assess the health and nutritional status of adults and children in the United States). In the European Union, based on data from EFSA (The European Food Safety Authority), about 140 mg/d, was intake.[18] In the EU and USA mainly flavan-3-ols flavonoid are consumed at higher level, mainly from tea, while intake of other flavonoids was considerably lower. [17][18]

Current *In-Vitro* Research Data-

Food and Drug Administration (FDA) and European Food Safety Authority (EFSA), has approved various health claims for flavonoids, and it also described flavonoid as a pharmaceutical drugs.[19][20][21] Flavonoid are show many types of activity (Biological and pharmacological activity) in *in-vitro* study. Like - Anti-Allergic[22], Anti-Inflammatory[22][23], Antioxidant[23], anti-microbial (antibacterial)[24][25], Antifungal and Antiviral[26][27], Anti-Cancer[23][28], Anti-Diarrheal[29], and also Anti-Diabetic activity[30].

Bioflavonoid act as a anti-diabetic drug-

According to (Ayman M. Mahmoud, et al 2016), Bioflavonoids are a group of polyphenolic compounds present in fruits, and also present in flowers and leaves of plants. Flavonoids act by modulating oxidative stress and inflammation. But at present time after several study, in this study bioflavonoid act as antioxidant, anti-inflammatory, **Anti-Diabetic** and hepatoprotective activities.[9]

CONCLUSION

In conclusion, the research highlights **Type-2 Diabetes Mellitus (T2DM)** as a critical global health challenge, representing approximately **95% of all diabetes cases**. The condition is primarily driven by **insulin resistance**, where body cells fail to use insulin effectively, eventually leading to hyperglycemia. With millions of people affected in countries like **China and India**, the need for effective management strategies is paramount. The sources suggest that **bioflavonoids**, particularly **Hesperidin**, offer a promising natural therapeutic approach6.... These polyphenolic compounds, found abundantly in **citrus fruits, tea, and dark chocolate**, possess significant **antioxidant, anti-inflammatory, and anti-diabetic properties**. They function by **modulating oxidative stress and inflammation**, which are key factors in the progression of diabetes. Because bioflavonoids exhibit **low toxicity** compared to other active plant compounds and are widely available in the human diet, they represent a safe and effective dietary intervention. Integrating these natural compounds into treatment regimens could significantly improve the **quality of life** for diabetic patients and help mitigate the rising global burden of the disease.

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