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EXPLORING THE POTENTIAL BENEFITS OF RESVERATROL IN MANAGING METABOLIC DISORDERS

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ABSTRACT

Metabolic disorders, including obesity, type 2 diabetes, and cardiovascular diseases, pose significant challenges to global public health. Despite advancements in therapeutic approaches, effective management remains elusive. Resveratrol, a polyphenolic compound abundant in various dietary sources such as grapes, red wine, and berries, has emerged as a potential therapeutic agent for metabolic dysfunction. This abstract synthesizes findings from a comprehensive review of the literature, highlighting the diverse mechanisms through which resveratrol exerts its beneficial effects on metabolic health. These mechanisms encompass modulation of insulin sensitivity, regulation of lipid metabolism, attenuation of inflammation, and enhancement of mitochondrial function. Furthermore, preclinical and clinical studies have demonstrated the efficacy of resveratrol supplementation in ameliorating metabolic parameters and improving overall metabolic health in both animal models and human subjects. However, challenges such as bioavailability and dosing regimens warrant further investigation. Overall, this literature-based abstract provides a nuanced understanding of the therapeutic potential of resveratrol in the management of metabolic disorders, laying the foundation for future research and clinical interventions in this field.

Keywords: Resveratrol, Diabetes, Grapes, Anthocyanins.

I. INTRODUCTION

Metabolic syndrome encompasses a cluster of disorders that collectively heighten the susceptibility to developing atherosclerotic cardiovascular disease, insulin resistance, type 2 diabetes mellitus, as well as vascular and neurological complications, including cerebrovascular accidents [(1).] Nearly a century ago, in 1923, Kylin provided early insights into the clustering of cardiovascular risk factors by describing the association among hypertension, hyperglycemia, and gout. Building upon this foundation, Vague further elucidated the concept in 1947 by demonstrating the common occurrence of visceral (central) obesity alongside metabolic abnormalities seen in cardiovascular diseases and type 2 diabetes mellitus (T2DM). However, the formal conceptualization of metabolic risk factor clustering originated from Gerald Reaven, a distinguished diabetologist. During the Banting memorial lecture in 1988, Reaven proposed that insulin resistance serves as a central feature in the pathogenesis of various chronic diseases, notably ischemic heart disease (IHD) and diabetes mellitus. He posited that insulin resistance leads to compensatory hyperinsulinemia and the clustering of metabolic abnormalities, including hyperinsulinemia, impaired glucose tolerance, elevated blood pressure, and dyslipidemia characterized by increased triglycerides and decreased high-density lipoprotein (HDL) cholesterol. Reaven hypothesized that this syndrome represents a significant risk factor for the development of IHD and Diabetes Mellitus [(2)].

Prevalence-

In 2019, the estimated global prevalence of type 2 diabetes mellitus (T2DM) was 43.8 million cases, while hypertension (HTN) accounted for 18.5 million cases, and non-alcoholic fatty liver disease (NAFLD) reached 1.2 billion cases.

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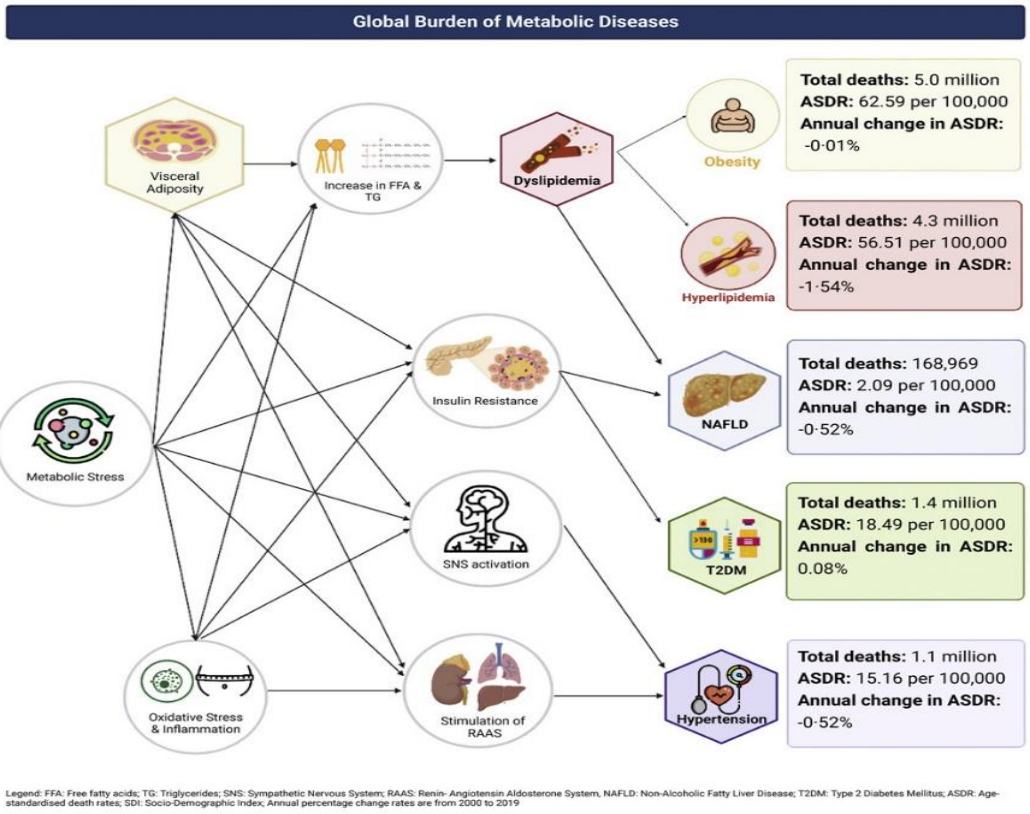

Fig 1 – Global Burden Of Metabolic Diseases [3]

However, global prevalence estimates for high low-density lipoprotein (HLD) and obesity were not available in the Global Burden of Disease (GBD) data. Analysis of trends from 2000 to 2019 revealed a steady increase in deaths attributed to metabolic disorders, with obesity showing the highest absolute burden, followed by HLD, T2DM, HTN, and NAFLD (Figure 1A). This trend was similarly reflected in Disability-Adjusted Life Years (DALYs) (Figure 1B). In terms of mortality, obesity accounted for the highest number of deaths, with 5.0 million in 2019, followed by HLD (4.3 million), T2DM (1.4 million), HTN (1.1 million), and NAFLD (168,969 deaths). Figure 2 illustrates that the greatest proportion of mortality related to metabolic diseases was attributed to obesity, accounting for 40.36% and 41.83% of deaths in males and females, respectively. Similarly, the majority of global DALYs attributed to metabolic diseases were associated with obesity, representing 43.76% and 47.85% of DALYs in males and females, respectively [3].

About Resveratrol-

Resveratrol was initially isolated in 1939 by Takaoka from the roots of Veratrum grandiflorum O. Loes (white hellebore) (Takaoka, 1939). It is hypothesized that the name "resveratrol" was derived based on its chemical structure and its plant origin: it is a resorcinol derivative, a polyphenol found in the resin of Veratrum species, and contains hydroxyl groups characteristic of alcohols [4]. Resveratrol gained significant attention due to the phenomenon known as the “French Paradox.” In the early 1990s, this term emerged from observations that French adults exhibited a relatively low incidence of coronary heart disease compared to their peers in other Western countries, despite a high dietary intake of saturated fatty acids. The French scientist Renaud attributed this paradox to the higher consumption of red wine. Subsequent research identified the high resveratrol content in wine as a potential contributing factor to the health benefits associated with red wine. Since then, interest in this natural compound has increased substantially [5].

Chemical Structure of Resveratrol-

Resveratrol is a stilbenoid polyphenol characterized by two phenol rings connected via an ethylene bridge. Its chemical structure, trans-3,5,4'-trihydroxystilbene, exists in two isomeric forms: *cis*- and *trans*-resveratrol. The *trans* form is more prevalent and is associated with various biological activities, including inducing cellular

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responses such as cell cycle arrest, differentiation, apoptosis, and inhibition of cancer cell proliferation. The formal IUPAC name of resveratrol is E-5-(4-hydroxystyryl)benzene-1,3-diol. Currently, various aspects of resveratrol chemistry are being studied. It exists as two geometric isomers: *cis*-(Z) and *trans*-(E), with the *trans* form capable of isomerizing to the cis form upon exposure to UV irradiation [6] .

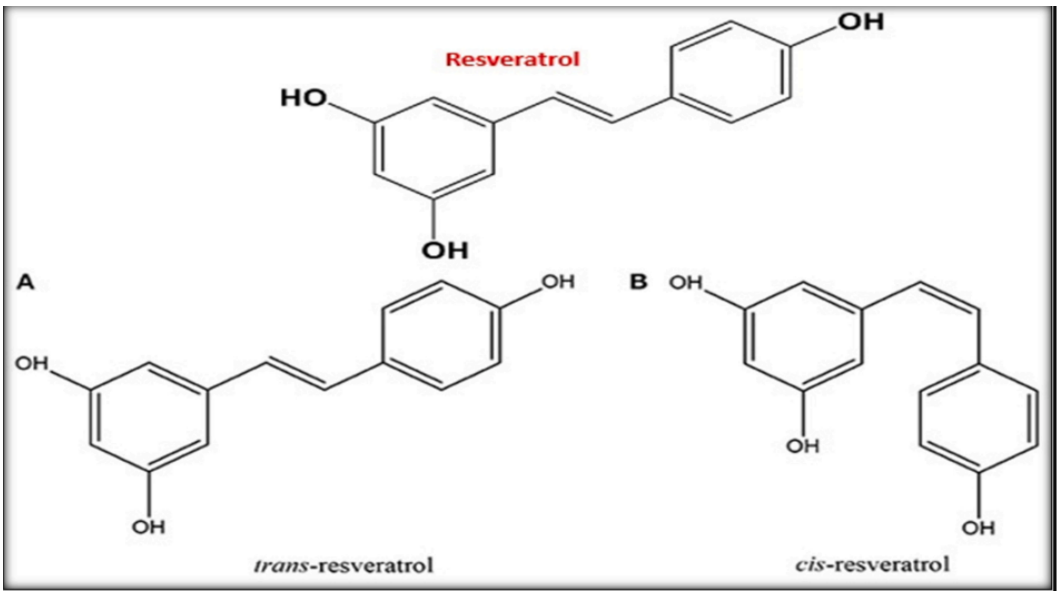

Fig 2- Resveratrol and its isomeric forms include trans-resveratrol (trans-RV; 3,5,4'-trihydroxystilbene) and the cis-isomer. (A) trans-RV (B) cis-RV [7] .

Clinical benefits-

Neurological disorders-

Neurological disorders, such as Alzheimer's disease (AD) and stroke, are believed to result from oxidative and inflammatory damage to the central nervous system (CNS). Resveratrol, known for its potent anti-inflammatory and antioxidative properties, has been proposed as a potential therapeutic agent for these neurological disorders. Furthermore, resveratrol modulates the activities of AMPK, SIRT1, and PGC-1α, which are metabolic regulators implicated in the onset of neurological conditions. While the precise mechanisms underlying AD development remain unclear, several biomarkers have been identified that characterize disease onset and progression, serving as potential therapeutic targets. For instance, the accumulation of amyloid-β (Aβ) plaques, driven by mutations in the amyloid beta precursor protein (APP) and apolipoprotein E (APOE) genes, along with increased inflammation and oxidative damage, have been associated with AD. Additionally, caloric restriction, which activates the deacetylase sirtuins most notably SIRT1, also activated by resveratrol has been shown to prevent the onset of neurological disorders. Clinical trials indicate that resveratrol effectively reduces biomarkers associated with AD and brain ischemic stroke, demonstrating sufficient bioavailability at administered dosages without significant adverse events [8].

Diabetes-

Resveratrol has demonstrated the potential to improve glycemic control and exhibit antioxidative properties in animal studies, prompting investigations into its use as a promising diabetes therapy. However, due to the limited number of clinical studies, small sample sizes, and conflicting data, the effectiveness of resveratrol remains uncertain. Resveratrol has been shown to improve glycemic control in humans, as reflected by glycated hemoglobin (HbA1c) levels, which serve as predictors of the microvascular and macrovascular complications associated with type 2 diabetes. A study by Bhatt et al. reported that daily resveratrol treatment for three months resulted in decreased HbA1c levels, systolic blood pressure, total cholesterol, and total protein, thus improving glycemic control. Although fasting blood glucose levels also decreased, the change was not statistically significant. These findings suggest that resveratrol could serve as a potential adjuvant in diabetes treatment. [8].

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Cancer preventive-

At lower doses, resveratrol functions as an anti-apoptotic and cardioprotective agent, while at higher doses it exhibits pro-apoptotic properties, inducing apoptosis in cancer cells. Resveratrol influences various intracellular mediators, impacting all three stages of oncogenesis: initiation, promotion, and progression. Depending on the tumor model, intracellular targets of resveratrol may include nitric oxide (NO), tumor suppressor p53, apoptosis regulators, cyclooxygenases, transcription factors, cyclins, calpains, caspases, interleukins, cathepsins, and others. Resveratrol has been demonstrated to suppress the proliferation of various tumor cells, including those of myeloid, breast, lung, liver, pancreas, prostate, skin, colon, and stomach origin. Due to its lipophilic nature, resveratrol may inhibit phase I enzymes (CYP family) in vivo, thereby preventing the initiation of oncogenesis [9].

Cardiovascular diseases-

Due to the increased incidence of cardiovascular diseases (CVDs), such as atherosclerosis, hypertension, stroke, ischemic heart disease, and heart failure, which are leading causes of global mortality and morbidity, extensive research is being conducted in this field. Several studies have demonstrated the anti-atherosclerotic, anti-hypertensive, anti-myocardial ischemia, anti-stroke, and heart failure effects of resveratrol (RSV). One cardioprotective mechanism of RSV is the enhancement of nitric oxide (NO) bioavailability. NO plays a crucial role in improving vasodilation and reducing platelet aggregation, leukocyte recruitment, and smooth muscle cell proliferation, all of which inhibit the formation and progression of atherosclerosis. Overall, the beneficial effects of RSV, through oxygen-derived radical scavenging or increased NO bioavailability in vitro, appear promising for combating CVDs [10].

Kidney disease-

Kidney disorders usually occur due to oxidative stress and inflammation. Polycystic kidney disease (PKD) is an autosomal dominant kidney disorder with mutations in polycystin-1 (PC1) and polycystin-2 (PC2) encoding genes (i.e., PKD1 and PKD2). These mutations are initiator cysts formation and progression of disease. Some of the pro-inflammatory factors are identified in cyst fluid or urine samples of PKD patients. Recently, it has been shown that inflammation and cytokine signaling play a significant role in PKD pathogenesis. For example, high concentrations of inflammatory factors (chemokines and cytokines) have been shown by Gardner et al. in kidney patients. Anti-inflammatory and antioxidant properties of RSV by inducing antioxidant enzyme production and modulating nuclear factors involved in the inflammation-oxidative stress cycle and established in numerous studies; therefore, it can act as a novel therapeutic agent in kidney disease treatments demonstrated that RSV acts as an anti-inflammatory substance, which delayed PKD progression through attenuation of NF-κB-induced inflammation [10].

Liver Disease-

Resveratrol has demonstrated protective effects on various liver diseases in multiple studies. Specifically, resveratrol mitigated non-alcoholic fatty liver disease (NAFLD) by upregulating the expressions of low-density lipoprotein receptor (LDLR) and scavenger receptor class B type I (SRB1) genes in the liver, or by regulating autophagy and reducing the activity of NF-κB through the restoration of its inhibitor, nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor α (IκBα). Additionally, resveratrol ameliorated high-fat diet (HFD)-induced fatty liver by downregulating adipose differentiation-related proteins and increasing the number of CD68+ Kupffer cells. Resveratrol's potential to improve NAFLD, chemical-induced liver injuries, fibrosis, and cirrhosis is attributed to its ability to modulate redox status, regulate lipid metabolism, reduce inflammation, and induce autophagy, involving various cytokines, chemokines, and transcription factors [11].

Obesity-

Obesity has become a severe global health issue. In mice with high-fat diet (HFD)-induced obesity, resveratrol significantly reduced body weight and fat mass, decreased leptin and lipid levels in plasma, modulated glucose and insulin metabolism, and restored immune function. These effects were mediated through the activation of PI3K/SIRT1 and Nrf2 signaling pathways, and the inhibition of transcriptional regulators such as the EP300 gene, which are involved in adipocyte differentiation, lipid storage, and metabolism. When administered to pregnant and lactating mice, resveratrol promoted the browning of white adipose tissue and thermogenesis in

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male offspring, with these health benefits persisting and preventing obesity later in life. Additionally, resveratrol protected against sarcopenic obesity by improving mitochondrial function and reducing oxidative stress via the PKA/LKB1/AMPK pathway. Resveratrol also had positive effects on obesity-related complications, such as reproductive dysfunction, including infertility and endocrine disorders. Overall, resveratrol has been shown to reduce body weight, regulate lipid deposition, modulate adipocyte gene expression, and promote the browning of white adipose tissue through the PI3K/SIRT1, Nrf2, PPAR-γ, TNF-α, and PKA/LKB1/AMPK signaling pathways. [11].

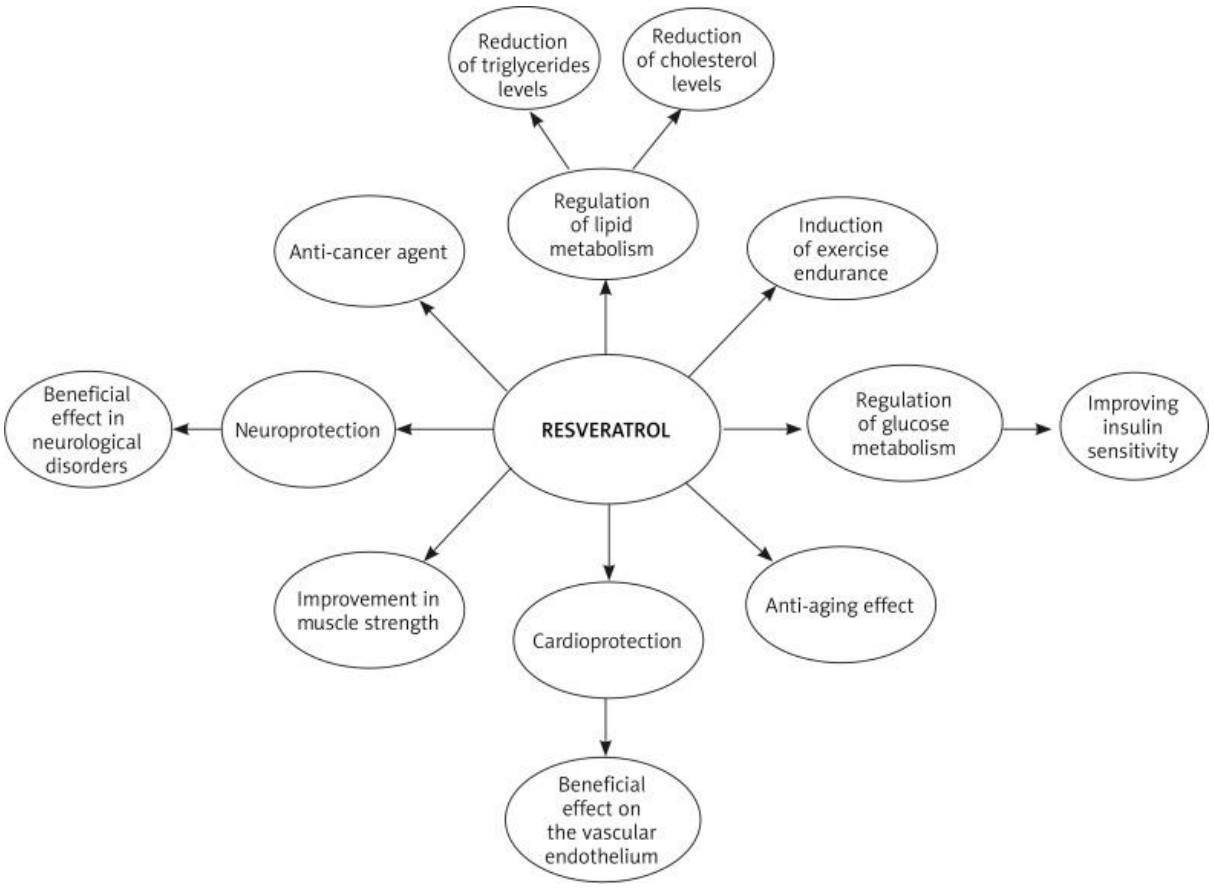

Fig 3- Action of Resveratrol [12].

Other Health Benefits-

Resveratrol & Skin-

Resveratrol is increasingly utilized in cosmetology and dermatology due to its numerous scientifically validated health benefits. This polyphenolic phytoalexin, abundantly found in red grapes and berries, has been shown to positively affect the cardiovascular system, lower low-density lipoprotein (LDL) levels, and inhibit cyclooxygenase activity. Additionally, resveratrol exhibits antiproliferative, anti-angiogenic, anti-inflammatory, antioxidant, and antimicrobial properties. Its popularity in cosmetology and dermatology is primarily due to its demonstrated ability to penetrate the skin barrier and its anti-aging effects. Formulations containing resveratrol have been shown to stimulate fibroblast proliferation and increase collagen III concentration. Resveratrol's affinity for estrogen receptors (ERα and ERβ) further enhances the production of collagen types I and II. Moreover, its antioxidant properties protect cells against oxidative damage from free radicals and UV radiation by reducing the expression of AP-1 and NF-kB factors, thereby slowing the process of photoaging. This study reviews the literature on resveratrol's skin care properties, including its dermal bioavailability, metabolism, and safety of application [13].

Sources-

The richest source of resveratrol was red wine, contributing 82.6% of the total. When categorized by food groups, the primary contributors were wines (98.4%), followed by grapes (1.1%), must and juices (0.5%), and

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finally peanuts and pistachios (less than 0.01%). For trans-piceid, the major sources were wines (98.7%), must and juices (0.7%), and grapes (0.6%). For trans-resveratrol, the identified food sources were wines (95.9%), grapes (3.8%), must and juices (0.3%), and peanuts, pistachios, and berries (0.03%). For cis-isomers, the primary contributors were wines, accounting for 99.9% and 99.7% of cis-resveratrol and cis-piceid, respectively, with must and juices contributing 0.1% and 0.3% correspondingly [14].

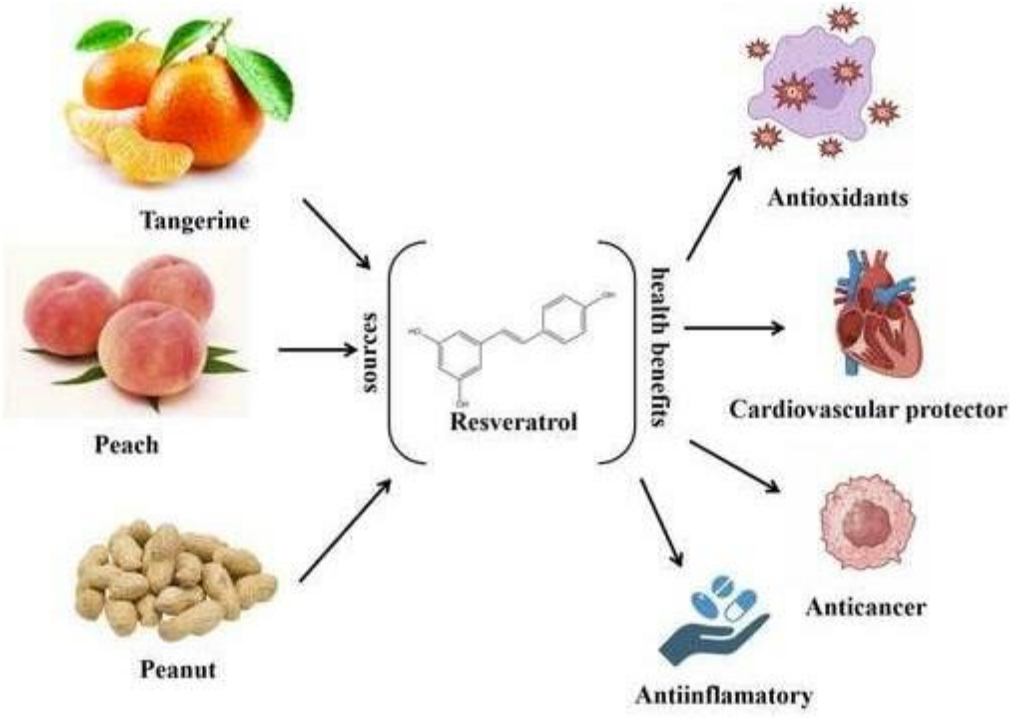

Fig 4- Rich sources of Resveratrol [15]

The Action of Resveratrol on Metabolic Disorders-

Resveratrol exerts beneficial effects on metabolic syndrome and related disorders through various mechanisms. Below, we summarize key targets of resveratrol in both healthy and diseased states:

1. SIRT1: The sirtuin family of proteins catalyzes the NAD+-dependent deacylation of acyl-lysine residues. Alterations in sirtuin expression are critical in several diseases, including metabolic syndrome, cardiovascular diseases, cancer, and neurodegeneration. Elevated levels of SIRT1 help manage conditions such as obesity, cardiovascular diseases, and neurodegeneration. Resveratrol activates SIRT1, yielding cardioprotective, antioxidant, and anti-inflammatory effects. SIRT1 transgenic mice exhibit features similar to those seen with calorie restriction.

2. AMPK: AMP-activated protein kinase (AMPK) is a key protein kinase that maintains cellular and systemic homeostasis. The health benefits of SIRT1 activation by resveratrol overlap significantly with those conferred by AMPK activation. AMPK functions as a nutrient sensor, regulating whole-body metabolism, coordinating metabolic reactions, and inducing inflammatory responses. Resveratrol can activate SIRT1, AMPK, and the Nrf2/antioxidant defense pathways, as demonstrated in a rat periodontitis model.

3. Renin-Angiotensin System (RAS): The RAS plays a significant role in metabolic syndrome. In Ang II-stimulated vascular smooth muscle cells (VSMCs), resveratrol treatment significantly reduced the number of senescence-associated β-galactosidase-stained cells and pro-fibrotic protein expression while increasing the expression of AT2R and MasR.

4. Other Mechanisms: Resveratrol has been shown to influence gut microbiota and their metabolic products, such as short-chain fatty acids and intraluminal lipids, thereby alleviating metabolic

syndrome. Additionally, resveratrol modulates mitochondrial function and dynamics, potentially regulating transcription factors that affect mitochondrial-related gene expression and altering mitochondrial physiology. Resveratrol also influences the transcriptional regulation of the NF-κB family of proteins and activates the Nrf2-Keap1 signaling pathway, which has been implicated in diabetic nephropathy. Anti-inflammatory actions are another major mechanism through which resveratrol exerts its effects on metabolic syndrome. (16).

II. CONCLUSION

In conclusion, resveratrol exhibits multiple beneficial effects on metabolic syndrome through various mechanisms. It improves glycemic control, modulates lipid metabolism, and enhances insulin sensitivity, thereby addressing key aspects of metabolic syndrome. Resveratrol's activation of SIRT1, AMPK, and Nrf2 signaling pathways contributes to its anti-inflammatory, antioxidative, and cardioprotective properties. Furthermore, resveratrol positively influences mitochondrial function and dynamics, modulates gut microbiota, and regulates adipocyte differentiation and lipid storage. Despite promising preclinical data, the clinical efficacy of resveratrol in treating metabolic syndrome requires further investigation due to the limited number of clinical trials, small sample sizes, and inconsistent results. Overall, resveratrol holds potential as a therapeutic agent for metabolic syndrome, warranting more comprehensive and large-scale clinical studies to confirm its effectiveness and elucidate the underlying mechanisms.

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III. REFERENCES

[1] Swarup S, Goyal A, Grigorova Y, et al. Metabolic Syndrome. [Updated 2022 Oct 24]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK459248/

[2] Bhalwar R. (2020). Metabolic syndrome: The Indian public health perspective. Medical journal, Armed Forces India, 76(1), 8–16. https://doi.org/10.1016/j.mjafi.2019.12.001

[3] Chew, N., Ng, C. H., Tan, D. J. H., Kong, G., Lin, C., Chin, Y. H., Lim, W. H., Huang, D. Q., Quek, J., Fu, C. E., Xiao, J., Syn, N., Foo, R., Khoo, C. M., Wang, J., Dimitriadis, G. K., Young, D. Y., Siddiqui, M. S., Lam, C. S., . . . Muthiah, M. (2023). The global burden of metabolic disease: Data from 2000 to 2019. Cell Metabolism, 35(3), 414-428.e3. https://doi.org/10.1016/j.cmet.2023.02.003

[4] Pezzuto, J. M. (2019). Resveratrol: Twenty years of growth, development and controversy. Biomolecules & Therapeutics, 27(1), 1–14. https://doi.org/10.4062/biomolther.2018.176

[5] Ponzo, V., Soldati, L., & Bo, S. (2014). Resveratrol: a supplementation for men or for mice? Journal of Translational Medicine, 12(1). https://doi.org/10.1186/1479-5876-12-158

[6] Salehi, B., Mishra, A., Nigam, M., Sener, B., Kilic, M., Sharifi-Rad, M., Fokou, P., Martins, N., & Sharifi-Rad, J. (2018). Resveratrol: a Double-Edged Sword in health Benefits. Biomedicines, 6(3), 91. https://doi.org/10.3390/biomedicines6030091

[7] Zhang, L., Li, C., Kakar, M. U., Khan, M. S., Wu, P., Amir, R. M., Dai, D., Naveed, M., Li, Q., Saeed, M., Shen, J., Rajput, S. A., & Li, J. (2021). Resveratrol (RV): A pharmacological review and call for further research. Biomedicine & Pharmacotherapy, 143, 112164. https://doi.org/10.1016/j.biopha.2021.112164

[8] Berman, A. Y., Motechin, R. A., Wiesenfeld, M. Y., & Holz, M. K. (2017). The therapeutic potential of resveratrol: a review of clinical trials. Npj Precision Oncology, 1(1). https://doi.org/10.1038/s41698-017-0038-6

[9] Kuršvietienė, L., Stanevičienė, I., Mongirdienė, A., & Bernatonienė, J. (2016). Multiplicity of effects and health benefits of resveratrol. Medicina, 52(3), 148–155.

https://doi.org/10.1016/j.medici.2016.03.003

[10] Koushki, M., Amiri-Dashatan, N., Ahmadi, N., Abbaszadeh, H., & Rezaei-Tavirani, M. (2018). Resveratrol: A miraculous natural compound for diseases treatment. Food Science & Nutrition, 6(8), 2473–2490. https://doi.org/10.1002/fsn3.855

[11] Meng, X., Zhou, J., Zhao, C., Gan, R., & Li, H. (2020). Health benefits and Molecular Mechanisms of resveratrol: A Narrative review. Foods, 9(3), 340. https://doi.org/10.3390/foods9030340

[12] Leis, K., Pisanko, K., Jundziłł, A., Mazur, E., Mêcińska-Jundziłł, K., & Witmanowski, H. (2022). Resveratrol as a factor preventing skin aging and affecting its regeneration. Postepy dermatologii i alergologii, 39(3), 439–445. https://doi.org/10.5114/ada.2022.117547

[13] Ratz-Łyko, A., & Arct, J. (2019). Resveratrol as an active ingredient for cosmetic and dermatological applications: a review. Journal of cosmetic and laser therapy : official publication of the European Society for Laser Dermatology, 21(2), 84–90. https://doi.org/10.1080/14764172.2018.1469767

[14] Zamora-Ros, R., Andres-Lacueva, C., Lamuela-Raventós, R. M., Berenguer, T., Jakszyn, P., Martínez, C., Sánchez, M. J., Navarro, C., Chirlaque, M. D., Tormo, M., Quirós, J. R., Amiano, P., Dorronsoro, M., Larrañaga, N., Barricarte, A., Ardanaz, E., & González, C. A. (2008b). Concentrations of resveratrol and derivatives in foods and estimation of dietary intake in a Spanish population: European Prospective Investigation into Cancer and Nutrition (EPIC)-Spain cohort. British Journal of Nutrition, 100(1), 188–196. https://doi.org/10.1017/s0007114507882997

[15] Xu, Y., Fang, M., Li, X., Wang, D., Yu, L., Ma, F., Jiang, J., Zhang, L., & Li, P. (2024). Contributions of common foods to resveratrol intake in the Chinese diet. Foods, 13(8), 1267. https://doi.org/10.3390/foods13081267.

[16] Hou, C., Tain, Y., Yu, H., & Huang, L. (2019b). The effects of resveratrol in the treatment of metabolic syndrome. International Journal of Molecular Sciences, 20(3), 535. https://doi.org/10.3390/ijms20030535