

**PROGRAM STUDI SARJANA FARMASI  
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Judul Skripsi : Pengaruh Polimorfisme Gen *CYP2C9* dan *TCF7L2*  
Terhadap Efek Samping Penggunaan Metformin dan  
Sulfonilurea pada Pasien Diabetes Melitus Tipe 2:  
Tinjauan Literatur

**ABSTRAK**

Diabetes Melitus tipe 2 (DMT2) merupakan penyakit metabolik kronis dengan prevalensi tinggi yang memerlukan terapi jangka panjang. Metformin dan sulfonilurea merupakan terapi lini pertama yang banyak digunakan, baik secara tunggal maupun kombinasi, namun perbedaan respons dan munculnya efek samping sering kali dipengaruhi oleh variasi genetik. Polimorfisme gen *CYP2C9* dan *TCF7L2* diketahui berperan penting dalam metabolisme obat dan regulasi glukosa, sehingga berhubungan dengan efektivitas terapi dan risiko efek samping. Penelitian ini menggunakan metode *narrative review* dengan pencarian artikel melalui *PubMed*, *ScienceDirect*, *Google Scholar*, dan *Semantic Scholar* berdasarkan kriteria inklusi dan eksklusi. Dari 1622 literatur yang diperoleh, sebanyak 15 artikel memenuhi kriteria dan dianalisis dengan persentase 1%. Hasil kajian menunjukkan bahwa polimorfisme *CYP2C9* (\*2 dan \*3) berhubungan dengan peningkatan risiko hipoglikemia akibat penurunan metabolisme sulfonilurea, sedangkan polimorfisme *TCF7L2* (rs7903146 dan rs12255372) dikaitkan dengan penurunan efektivitas sulfonilurea serta meningkatnya risiko kegagalan terapi. Selain itu, kombinasi metformin dan sulfonilurea pada pasien dengan variasi genetik tertentu juga dapat menimbulkan efek samping lain, seperti gangguan gastrointestinal dan resistensi obat. Terdapat jenis-jenis varian pada gen *CYP2C9* seperti varian \*2, \*3, dan varian 13. Sedangkan, pada gen *TCF7L2* terdapat varian seperti varian rs7903146 dan rs12255372.

**Kata Kunci: Diabetes Melitus Tipe 2, CYP2C9, TCF7L2, Efek Samping Metformin, Sulfonilurea**

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Title : *The Effect of CYP2C9 and TCF7L2 Gene Polymorphisms on the Side effects of Metformin and Sulfonylurea Use in Type 2 Diabetes Mellitus Patients: A Literature Review*

**ABSTRACT**

*Type 2 diabetes mellitus (T2DM) is a chronic metabolic disease with a high prevalence that requires long-term therapy. Metformin and sulfonylureas are widely used first-line therapies, either alone or in combination, but differences in response and the incidence of side effects are often influenced by genetic variations. Polymorphisms of the CYP2C9 and TCF7L2 genes are known to play important roles in drug metabolism and glucose regulation, thus being related to therapeutic efficacy and the risk of side effects. This study used a narrative review method with a search for articles through PubMed, ScienceDirect, Google Scholar, and Semantic Scholar based on inclusion and exclusion criteria. Of the 1,622 literatures obtained, 15 articles met the criteria and were analyzed at a percentage of 1%. The results showed that CYP2C9 polymorphisms (\*2 and \*3) were associated with an increased risk of hypoglycemia due to decreased sulfonylurea metabolism, while TCF7L2 polymorphisms (rs7903146 and rs12255372) were associated with decreased sulfonylurea efficacy and an increased risk of therapy failure. Furthermore, the combination of metformin and sulfonylureas in patients with certain genetic variants can also cause other side effects, such as gastrointestinal disturbances and drug resistance. Variants in the CYP2C9 gene include \*2, \*3, and \*13. Variants in the TCF7L2 gene include rs7903146 and rs12255372.*

**Keywords:** *Type 2 Diabetes Mellitus, CYP2C9, TCF7L2, Side Effects Metformin, Sulfonylurea*