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generic risperidone, although there were prescribing restrictions for long-acting injectable risperidone in Austria and Belgium. As a result, no change in its utilization after generics reimbursed. Overall, high utilization of generic versus originator risperidone once available. Appreciable reduction in the price of generic risperidone once it became available limited the extent of any subsequent increase in AAP expenditure despite increasing utilization.

Conclusion: No apparent effectiveness or safety problems with generic risperidone. Authorities cannot rely on a spillover effect from other disease areas to change physician prescribing habits, exacerbated on this occasion by the need to tailor treatment approaches with different AAPs having different mechanisms of action and appreciable variability in their effectiveness and side-effects between patients Consequently, specific demand-side measures are needed to encourage the prescribing of generic AAPs first line where appropriate, exacerbated by the complexity of these disease areas. Likely in any event that there will be limited influence of any measures in changing subsequent physician prescribing habits when managing patients with schizophrenia or BPD compared with acid-related stomach disorders or hypercholesterolemia as a greater need to tailor treatments. Generally no specific measures planned by these authorities to influence future prescribing habits with further generic AAPs becoming available.

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PP263—IMPORTANCE OF TDM, PHENOTYPING AND GENOTYPING DURING INTOXICATION WITH VENLAFAXINE

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Introduction: Antidepressive drug venlafaxine belongs to the serotonine and norepinephrine reuptake inhibitors. It is primary metabolized by CYP2D6 to its active metabolite O-desmethylvenlafaxine and by CYP3A4 to N-desmethylvenlafaxine. The range 0.3-5.2 for O-desmethylvenlafaxine/venlafaxine ratio was estimated for extensive and intermediate metabolizers.

Patients (or Materials) and Methods: There is described intoxication of woman (41 years) treated by combination therapy venlafaxine 150 mg/d, mianserine 60 mg/d, clonazepam 1 mg/d, and olanzapine 10 mg/d. TDM of these substances was provided using LC-MS/MS method to estimate phenotype of venlafaxine and to compare with genotype.

Results: On admission, toxic plasma level of venlafaxine was found (2638 ng/mL) and after reduction of the dose to 75 mg/d plasma level was estimated in therapeutic range (364 ng/mL). The ratio O-desmethylvenlafaxine/venlafaxine was estimated between 0.005 and 0.016 showing poor metabolizator. Genetic examination detected homozygotes deletion of the gene CYP2D6 *5/*5 and explained phenotype. Plasma level of olanazapine was found in therapeutic range, plasma level of clonazepam was found below therapeutic range.

Conclusion: The ratio of the metabolite to the parent substance (phenotype) allows us to detect any deviation in the metabolism of drugs which can be subsequently explained by determination of genotype. Therapeutic drug monitoring contributes to the optimalization of pharmacotherapy in the case of psychotropic drugs.

Disclosure of Interest: None declared.

PP264—4-METHYLESCULETIN A DUAL ACTING INHIBITOR OF ACETYLCHOLINESTERASE AND XANTHINE OXIDASE

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Introduction: Alzheimer's disease is a neurodegenerative disorder associated with depletion of acetylcholine in neuronal terminals with increased oxidative stress in cells resulting in neuroinflammation. Inhibiting acetylcholine esterase (AchE) increases the concentration of neuronal acetylcholine. Further xanthine oxidase (XO) is an important source of free radicals and plays an important role in oxidative stress associated with neuroinflammation. Thus, a dual acting inhibitor of AchE & XO can be a good candidate for the treatment of neurodegenerative disorders like Alzheimer's. The aim of this study is to explore the inhibitory potential of 4-methyl esculetin against both AchE and XO.

Patients (or Materials) and Methods: The X-ray crystal structures of rivastigmine bound to acetylcholinesterase (AChE) (PDB 1GQR) and quercetin bound to xanthine oxidase (XO) (PBD 3NVY) were obtained from the Protein Data Bank. The proteins were prepared for the docking studies with the Protein Preparation Wizard in the Schrödinger Suite 2012 (Schrödinger LLC, USA). The ligand 4-methyl esculetin (4-ME) was docked into the target proteins AhcE and XO and binding poses ranked by Glide Score (SP). The inhibitory activity of 4-ME towards AchE was measured by an in vitro assay using rat brain AchE, and inhibition of XO was done using crude XO obtained from rat liver tissue.

Results: The docking studies revealed that 4-methyl esculetin binds in a similar fashion to both AChE and XO and makes identical interactions as the native ligands (rivastigmine for AchE & quercetin for XO). The Glide Score for 4-methyl esculetin (–6.97 for AchE and –7.78 for XO) also does not differ significantly in both targets; hence, it can be said with confidence that 4-ME should exhibit comparable potency towards the 2 protein targets. This is well substantiated by in vitro enzyme assays that confirmed the equal inhibitory properties of 4-ME towards both the target *viz.* AchE and XO. Kinetic studies showed that 4-ME acts as a competitive inhibitor against XO while exhibiting mixed type inhibition toward AchE.

Conclusion: The results of the present study indicate that a combination of both AchE and XO inhibitory properties for 4-ME could make it a useful asset in the management of Alzheimer's disease.

Disclosure of Interest: None declared.

PP265—ATTENUATION OF ALUMINIUM INDUCED NEURODEGENERATION BY 4-METHYLESCULETIN

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Introduction: Aluminium is a potent neurotoxin and has been associated with Alzheimer's disease (AD). Prolonged aluminium exposure induces oxidative stress and contributes to the development of neurodegeneration. Current treatment modalities for AD provide only symptomatic relief, thus necessitating the development of new drugs with multiple targeting strategies. The aim of the study was to demonstrate the protective effect of chronic administration of 4-methylesculetin (4-ME) against aluminium-induced cognitive dysfunction and oxidative damage in rats.

Patients (or Materials) and Methods: Wistar rats (180–200 g) were divided into 6 groups (n = 6). Group I was the control group and group II received aluminium chloride (100 mg/kg PO) for a period of 42 days. Group III and IV received 4-ME (50 and 100 mg/kg PO) daily 1 hour before aluminium chloride (100 mg/kg PO) for 42 days while groups V and VI received only 4-ME (50 and 100 mg/kg PO) daily for 42 days. On the 21st and 42nd day, behavioral studies