Tamoxifen has been widely used as the standard adjuvant therapy for breast cancer patients with oestrogen receptor-positive status, especially in the high-risk pre- and postmenopausal women. However, 30 to 50% of ER-positive breast cancer patients do not respond to tamoxifen therapy. Major challenges to effective tamoxifen treatment include drug resistance, and adverse events. Thus, this study aims to investigate the impact of pharmacogenomics and metabolomics in monitoring the efficacy of tamoxifen treatment in BRCA patients. A total of 95 tamoxifen-treated patients, and 11 untreated breast cancer patients from three major Malaysian ethnic groups (Malay, Chinese and Indian) were recruited. However, only 84 tamoxifen-treated patients with completed clinical data were included for clinical association analysis. Blood and plasma samples were collected to obtain DNA, RNA, and metabolites, and clinical data of the patients were also collected. Investigations proceed with the genotyping of CYP2D6 and ABCB1 using multiplex allele specific PCR (ASPCR) approach. Patients carrying CYP2D6 *10/*10 and heterozygous null allele (IM) showed higher risks of developing recurrence and metastasis (OR, 13.14; 95% CI, 1.57 – 109.94; P = 0.004) compared to patients with CYP2D6/*1 and */*10 genotypes. Patients with homozygous CC genotype of C3435T had shown to have shorter recurrence time. Patients who were CYP2D6 IM and homozygous CC genotype of C3435T have statistically significant higher risks of recurrence (P = 0.002). Similarly, median time to recurrence in these patients was only 12 months (95%CI = 0.79 - 23.2) compared to those without this combination, which was 48 months (95%CI = 14.7 - 81.2). Patients with CYP2D6 IM and homozygous CC genotype of ABCB1 C3435T have shorter times to recurrence. The expression of oestrogen receptor-α and oestrogen receptor-β from the samples were quantitated using Real-time PCR. Absolute quantification of ERs reveals that the over-expression of ER-α in peripheral blood has positive correlation with the expression of ER-α in breast cancer tissue. The developed method would be useful as it is less invasive, and can be used to monitor a patient’s progress towards disease and drug therapy. Furthermore, the patients were also subjected to detonating high performance liquid chromatography (dHPLC) analysis to navigate the entire exon region of ER-α. There were a total of 3 variants sites detected and further analysis on ER-α SNPs revealed that CC genotype of C325G causes an increased risk of recurrence (P = 0.027). Global metabolic profiling was performed by Quadrupole Time-of-Flight (Q-TOF) in conjunction with multivariate data analysis and pathway analysis. A total of eight groups of compound were detected to have potentials to be developed into biomarkers. Pathway analysis showed that steroid hormone biosynthesis, aminoacyl-tRNA biosynthesis, tryptophan metabolism, fatty acid metabolism, and sphingolipid metabolism were affected in BRCA patients. This pilot study demonstrates that the integration of pharmacogenomics and metabolomics into conventional therapeutic drug monitoring could enhance the characterization of prognosis as well as the patients’ response towards therapy. This would allow more personalized treatment to patients, thus allowing better chances of success in individual therapy.

The leaves of *S. polyanthum* (Myrtaceae) and barks of *O. sumatrana* (Datiaceae) were investigated for their chemical constituents, antioxidant and cytoprotective activities. Their aqueous extracts were first subjected to acidic hydrolysis and the organic layers were dissolved in water and partitioned using hexane, ethyl acetate (EtOAc) and n-butanol (BuOH). Six compounds (betulinic acid, ellagic acid, kaempferol, myricetin, quercetin, and β-sitosterol) were isolated and identified from the EtOAc and BuOH extracts of *S. polyanthum* and four compounds (quer cetin, kaempferol, rutin, bryonolic acid) were purified from the n-butanol extract of *O. sumatrana* by means of MPLC and HPLC. The structures of the above compounds were determined by comparing their NMR and LCMS-TOF data with reported values. The structure of betulinic acid (EC50 = 26.7 ± 0.74) only marginally quenched DPPH radical but ellagic acid, myricetin, quercetin, rutin and kaempferol (92.4 ± 3.82, 74.1 ± 1.29, 76.04 ± 2.63, 76.8 ± 1.11 and 71.22 ± 1.09 (μM), respectively) showed strong DPPH radical scavenging activity. The isolated compounds from *S. polyanthum* and *O. sumatrana* (myricetin, ellagic acid, betulinic acid, β-sitosterol, rutin, quercetin, kaempferol and bryonolic acid) were tested for their cytotoxic effects towards three types of cells including normal human embryonic liver (WRL-68), normal green monkey kidney (Vero) and human hepatocarcinoma (HepG2) cell lines. The cells were treated with different concentrations of the compounds and the results showed that the compounds from *S. polyanthum* and *O. sumatrana* were non-toxic towards normal cells. However, betulinic acid and bryonolic acid had high cytotoxicity towards HepG2 cells. Next, the cytoprotective effects of the isolated compounds against hydrogen peroxide-induced WRL-68 and Vero cells were investigated. Quercetin, kaempferol, myricetin, ellagic acid, betulinic acid, β-sitosterol and bryonolic acid showed significant protective effects compared to control against oxidative stress-induced WRL-68 and Vero cells. Furthermore, betulinic acid and bryonolic acid showed higher protective effect compared to ellagic acid, kaempferol, myricetin and quercetin and the activities of the antioxidative enzymes such as superoxide dismutase (SOD) and catalase (CAT) were enhanced in a dose-dependent manner. In conclusion, this study demonstrated that most compounds from *S. polyanthum* and *O. sumatrana* were cytoprotective against oxidative stress induced by H2O2 with betulinic acid and bryonolic acid having the highest potential to be developed to be used as anticancer candidates and alternative medicine.