Statistical analysis

All results are expressed as mean ± standard deviation (n = 3). The significance of difference was calculated by Duncan's new multiple range test, and values $P < 0.05$ were considered statistically significant.

RESULTS

Hypouricemic activities in hyperuricemic rats

An experiment was conducted to examine the hypouricemic effects of TA on the plasma uric acid (P_{UA}) of hyperuricemic rats. The concentration of uric acid of each plasma sample at different time points was determined after oral administration and point 0 min is from TA but 1 h from PO injections. The hypouricemic effects of HE, EA, BuOH, and water fractions on PO-induced hyperuricemic rats are shown in Figure 3. IP injections of PO markedly increased the P_{UA} levels, and reached a C_{max} of 2.63 ± 0.08 mg/dl after 2 h, followed by a slow decrease in P_{UA} levels. The time course of response of P_{UA} levels in hyperuricemic animals was consistent with the previous report.[18] Compared with the PO group, the remaining four groups exhibited the significant reducing effects of TA on uric acid in hyperuricemic rat plasma after TA administration within 2.5 h ($P < 0.05$). Based on the reducing trend of uric acid, TA-EA showed strong XO inhibition 3.5 h after administration. Phytochemicals isolated from the most inhibitory extracts of TA, TA-EA, were then examined for their potential effects of XO inhibitory activities. Recently, Xu *et al*. reported that the administration of Rhizoma smilacis glabrae extract (1 ml/100 g) in hyperuricemic rats significantly reduced serum UA levels within 12 h.[14] The comparison of their results in lowering P_{UA} with ours indicates that TA extracts exhibit remarkable hypouricemic effects [Figure 3].

XO inhibitory activities of phytochemicals from TA extracts

The XO inhibitory activity of major phytochemicals from TA extracts was compared with allopurinol, which is clinically used as an XO inhibitor, as shown in Table 1. In the presence of test samples, AR1–AR12 obtained from the EA fraction at a concentration of 200 μg/ml, AR11 (bracteanolide A) exhibited the best XO inhibitory activity (71.3%), followed by AR10 (3-(3′,4′-dihydroxyphenyl)-butenolide) (50.0%); other compounds showed weak inhibitory effects, with percent inhibition values from 3.8% to 43.3% at a dose of 200 μg/ml. The IC_{50} values of AR11 and allopurinol were measured to be 76.4 and 0.46 μg/ml, respectively. These data suggest that the butenolide plays a very important role in XO inhibition, which is similar to that the acyl group obtained by Ngoc *et al*. derived from *Cinnamomum cassia* (*Lauraceae*) twigs, and is an essential structural component that helps determine the XO inhibitory activity.[13] Others yield weak or negligible inhibitory activity against XO [Table 1].

DISCUSSION

It is noteworthy that two hydroxybutenolides, bracteanolide A (AR11) and B (AR12) were isolated, identified, and first reported in the plant of study from *Murdannia bracteata* (*Commelinaceae*) using nitric oxide (NO) production assay.[19] The extract bracteanolide A was found the most potent and selective for inducible NO synthase, which may have potential anti-inflammatory properties. Moreover, our studies showed that bracteanolide A (AR11) was found to inhibit XO *in vitro*.

CONCLUSION

To the best of our knowledge, this is the first report on the scientific rationale of TA for anti-hyperuricemic medicinal use. Based on the results presented here, 12 compounds isolated from the TA-EA fraction of TA were evaluated for their XO inhibitory activity, and TA extracts were found to possess *in vivo* hypouricemic effects. The effective compound bracteanolide A (AR11), isolated from TA extracts, could be developed as a potent XO inhibitor.

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Conflicts of interest

There are no conflicts of interest.

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