Isolation and identification of the metabolites of Sudanese medicinal plants and synthesis of flavonoid glycosides

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博士論文内容の要旨

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論文題目（外国語の場合は，その和訳を併記すること。）

Isolation and identification of the metabolites of Sudanese medicinal plants and synthesis of flavonoid glycosides

（スーダン産薬用植物の代謝物の単離と同定およびフラボノイド配糖体の合成）

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The study aims to isolate and identify the metabolites that possess pharmacological and biological properties that have therapeutic benefits in treating diseases from important medicinal plants in Sudan namely *Striga hermonthica* and *Solenostemma argel* that used as a resource of pharmaceutical manufacture to provide useful medicine. The synthesis of complex molecules identical to the naturally occurring compounds, particularly synthesis of flavonoid glycosides (kaempferol 3−*O*−neohesperidoside) is the second purpose.

Chapter 2: Extraction, purification, isolation and identification of flavonoids of the ethyl acetate extract of the whole plant of the *Striga hermonthica*

S. hermonthica, commonly known as purple witchweed, is a hemi−parasitic plant, which is devasting to major crops such as rice (*Oryza sativa* L.), millet (*Pennisetum glaucum* (L.) Leeke), maize (*Zea mays* L.) and sorghum (*Sorghum bicolor* L. Moench). Beside its parasitic effect *S. hermonthica* is known as a medicinal plant in some parts of Africa, and it has been used in folk medicine for years to treat many ailments such as leprosy, leprous ulcers and pneumonia. In this chapter, it was identified the major flavonoids in the *S. hermonthica* plant. The whole plant has been dried at room temperature, coarsely grinded, and extracted with two extraction techniques. Firstly, the dried plant has been extracted with hot continuous extraction using Soxhlet extractor and MeOH at 50 °C, yielded 20% of the crude extract. Then separation of the crude extract with liquid−liquid separation in acidic and basic conditions followed by purification with preparative TLC led to isolate two flavonoids, which were analyzed with ^{1}H NMR spectroscopy and characterized as flavones and identified based on the comparison to reported data as chrysoeriol (0.01%) and apigenin (0.003%). Secondly, the dried plant was soaking with 80% aqueous methanol at room temperature for seven days furnishing 20% of the crude extract. By the comparison, it was observed that the hot and cold extraction techniques afforded the same yield of the extractable matter. The dried extract was separated with liquid−liquid partitioning using neutral conditions by dissolving the crude extract with 20% aqueous ethanol. The flavonoids of ethyl acetate extract have been purified and isolated with silica gel column chromatography and plate coated silica gel and identified with NMR spectroscopy as chrysoeriol, apigenin, luteolin, and apigenin 7−*O*−β−glucoside, and their yield % in the dried plant were 0.0004, 0.026, 0.004, and 0.003%, respectively. As a result, we observed that the liquid−liquid partitioning in neutral conditions enhanced the isolation of the flavonoids.

Chapter 3: isolation and characterization of the metabolites of the ethyl acetate extract of the *Solenostemma argel leaves*

S. argel is well−known as a medicinal plant in some parts of Sudan, where it is used as an anti-spasmodic, anti−diabetic and anti-inflammatory because of its many useful secondary metabolites. In this chapter, it was identified and quantified the major metabolites of ethyl acetate extracts of *S. argel* leaves. Dried leaves of *S. argel* were macerated, extracted and subjected to liquid−liquid partitioning. The metabolites of the ethyl acetate extract were purified and isolated using a combination of chromatographic techniques (silica gel column chromatography and preparative thin layer chromatography). The structures of the isolated compounds were identified using infrared and nuclear magnetic resonance spectroscopy. The results showed that the three major metabolites of the ethyl acetate extract of *S. argel* leaves were kaempferol with 0.1% yield, kaempferol-3−*O*−β−D−glucopyranoside (astragalin) with 6.0% yield and kaempferol−3−*O*−[α−L−rhamnopyranosyl (1→2)−β−D−glucopyranosyl (Kaempferol 3−*O*−neohesperidoside) with 16% yield.

Chapter 4: Synthetic study of Kaempferol 3−*O*−neohesperidoside

Kaempferol 3−*O*−neohesperidoside has been isolated from *S. argel.* Synthesis of such compounds was achieved by synthesis of the disaccharide bromide **30** then aglycone flavonol. Disaccharide bromide **30** would be synthesize from the glucosyl acceptor **27** and rhamnosyl donor-**28** promoting by the Lewis acid TMSOTf. In this chapter, rhamnosyl donor **28** was synthesized from the known rhamnose in excellent yield (95 %) as a pure α anomer. Glucosyl acceptor synthesized by the epoxidation of the commercial 3,4,6-Tri-*O*-benzyl-D-glucal **26** by *m*CPBA−KF forming a mixture of pure sugar epoxide **48** in good yield 80% and high stereoselectivity (α/β = 6/1) when using 1:5 molar ratio of **26**: *m*CPBA−KF. In addition, the reaction conditions of the preparation of *m*CPBA−KF were optimized and good results were achieved when using 1:4 molar ratio *m*CPBA:KF in anh.CH_2Cl_2. Thereafter, **48** ring opening with acetic acid led to form glycosyl acceptor **27** which is successfully glycosylated with the rhamnose donor **28** in the presence of TMSOTf furnishing a mixture of the disaccharide **29** in 60% (α/β = 1/2) which is easily transformed to pure α anomer of disaccharide bromide **30** in 12% using HBr/AcOH (25%)**.** Also, **30** was successfully synthesized for the first time from disaccharide *m*-chlorobenzoate **47** in 16%. **47** is also synthesized for the first time in this study by the glycosylation reaction of 1−*O*−*m*-chlorobenzoyl−3,4,6−tri−*O*−benzyl−D−glucopyranose **43** and rhamnosyl TCA donor **28** using TMSOTf as glycosidic agent at -20 °C for 30 min yielded 32% (α/β = 1/4) of **47**.