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AQUEOUS BALANITES ROXBURGHII: A CLEAN AND GREEN BIOCATALYST FOR SYNTHESIS OF SULFONAMIDES

Vinod R. Kadu[a*], Gajanan R. Pandhare[b], Somnath S. Gholap[c] and Amol K. Kharde[a]

[a]*Department of Chemistry, Arts, Science and Commerce College, Kolhar, Tal.- Rahata, Dist.- Ahmadnagar, Pin-413712 (MS), India.*
[b]*Post graduate Department and Research centre, Padmashri Vikhe Patil College, Pravaranagar, A/P-Loni kd, Tal.- Rahata, Dist.- Ahmadnagar, Pin-413713 (MS), India.*
[c]*Department of Chemistry, Arts, Commerce and Science College, Rahata, Tal.- Rahata, Dist.- Ahmadnagar, Pin-423107 (MS), India.*
**Correspondence: vinodkaduv2@gmail.com*

ABSTRACT:
Sulfonamide group is a versatile group introduced as the key core for diverse bio-activities as antibacterial sulfonamides and non-anti-bacterial sulfonamides in drug industry. Two component one pot synthesis of sulfonamides have been effectively carried out using aqueous solution of natural surfactant viz; *Balanites Roxburghii* which is commonly known as hingan. The present study has been employed by environmentally available *Balanites Roxburghii* as catalyst at room temperature. The present methodology of synthesis of sulfonamides comes out with advantages like economically feasible, simple and biocompatible catalytic system states safely production of different sulfonamide derivatives on bulky scale.

KEYWORDS: Sulfonamide, natural surfactants, *Balanites Roxburghii,* hingan economically feasible, simple and biocompatible catalytic system.

INTRODUCTION:

The newer organic synthesis which is carried out by naturally available catalyst has great importance in the field of green chemistry. The naturally occurring catalyst will accompanied the organic synthesis may be whispered as environmentally benign. There is need for achieving great goals through green chemistry in the field of organic synthesis by building useful organic cores for bulky drug molecules that are presently synthesised by disadvantageous methodology. Naturally abundant available materials like clays[i], enzymes[ii] and surfactants[iii] are extensively applied for different routes of synthesis of organic targets. These naturally occurring materials are promising substitutes for the hazardous organic solvents and catalysts that are presently practised in organic synthesis. Presently used solvents and catalysts in the organic conversions are with disadvantages like expensiveness, short of biodegrability, tedious work-up procedures, use of halogenated organic solvents, use high temperature to get required yield organic compound etc. There are

also some different naturally occurring biochemicals giving distinctive classified active biocatalyst used in organic procedures[iv-vi]. These biocatalyst have gained much more attention of current researcher in the field of organic chemistry through pollution free and eco-friendly protocols[vii] as per the Green Chemistry principles. In this perspective, the plant cell culture of *Daucus carota* root[viii-xiii], soaked *Phaseolus Aureus* (green grams)[xiv], coconut juice (*Cocos Nucifera*)[xv] has been effectively used as catalysts for selective reduction of ketones, aq. extract of *Acacia concinna* has been utilized as reaction medium for the synthesis of 3-carboxycoumarins and Cinnamic acids[xvi], acylation of amines[xvii] and synthesis of aryl-hydrazones[xviii].

Sulfonamides are useful in the field of medicinal chemistry as its core is utilized in building up bulky drugs. Sulfonamides and their derivatives are widely used for HIV protease inhibitor (A) amprenavir[xix], antibacterial activity[xx], anti-carbonic anhydrase[xxi], hypoglycaemic[xxii] , antitumour[xxiii] , anti-thyroid[xxiv] and diuretic (B) Hydrochlorothiazide, (C) Hydroflumethiazide, (D) Quinethazone and (E) Metolazone[xxv], (Figure 1).

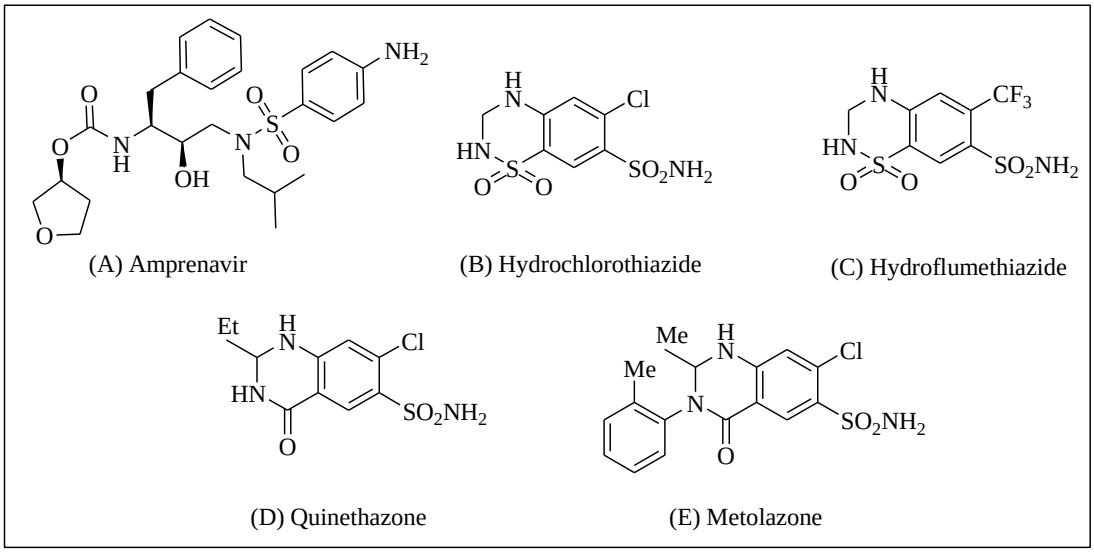


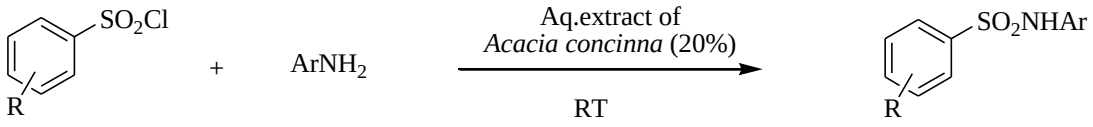
Figure 1. Chemical structure of some pharmacologically active sulfonamide derivatives

Sulfonamides were synthesised from sulfonylbenzotriazoles and different amine was general and efficient procedure[xxvi]. Now a days they are synthesised by oxidation of thiols to sulfonyl chlorides which on further reaction with amines yields sulfonamide is reported[xxvii]. Simply sulfonamides are also synthesised from sulfonic acids[xxviii]. Sulfonic acid on reaction with isocyanate also yields sulfonamides at room temperature[xxix].

Acacia concinna is generally known as Shikakai which has family Leguminosae and originates in tropical region of southern Asia. The fruits of *Acacia concinna* have cleansing property due to the presence of saponins that are foaming agents. These saponis produces leather when shaken in aqueous solutions. The fruit is known to have 10-11.5% saponins and their structure has been reported.[xxx,xxxi] These saponins resolves similar surfactant properties as that of dodecyl benzene sulphonates.[xxxii] The aqueous extract of these pods of *Acacia concinna* shows acidic pH which is due to the 'acacic acid' found in the solution.[xxxiii] Encapsulation of the reactants in micellar cages drives the equilibrium toward the product side by giving out the water molecule out of its interior yields of products (Figure 2). The action of micellar cages in formation of product excited us to use aqueous Acacia concinna solutions as an efficient and eco-friendly acidic surfactant catalyst for the synthesis of sulfonamide derivatives.

RESULT AND DISCUSSION:

Current methodology presents economical, simple and greener pathway for synthesis of sulfonamide catalyzed by aq. extract of *Acacia concinna* pods which in continuation of our ongoing research on development of newer synthetic method for bioactive compounds.[xxxiv-xxxix] Different sulfonamides (**3**) were synthesised using various aromatic sulfonyl chlorides (**1**) and aromatic amines (**2**) (Scheme 1). Synthesis of sulfonamides by current approach does not involve use hazardous organic solvents, and no tedious reaction workup. Green chemistry principles are followed in the current methodology.[xl-xli]



1 **2** **3**

Scheme 1. Natural surfactant catalyzed synthesis of sulfonamide derivatives

Reaction of benzene sulfonyl chloride (1mmol) and aniline (1mmol) in 10 mL aqueous extract of *Acacia concinna* pods (10% w/v) at room temperature was carried out in order to ensure the catalytic effectiveness of present natural surfactant and we are good yield of product **3a.** The result encouraged us for optimisation of concentration of aqueous solutions of *acacia concinna* pods. Optimisation study concluded that that 20% of the catalyst was sufficient to get highest yield of the product **3a** (>95%). Increasing concentration of *Acacia concinna* pods (25%, 30%, 35% and 40%) did not affect the yield of the final product. Hence, 20% (w/v) aqueous extract of *Acacia concinna* pods and 10 mL volume was selected as optimized to drive the reaction (Table 1). Different sulfonamide derivatives are synthesis at reaction time and in good yields as in Table 2.

Table 1. Optimization of catalyst concentration.

Entry	Catalyst concentration %(w/v)	Time (hr)	Yield(%)[a]
1.	10	2.5	92
2.	20	1.5	97
3.	25	1.5	95
4.	30	2	95
5.	40	2	92
6.	--	12	NR[b]

[a]Isolated yield of **3**. [b]No Reaction

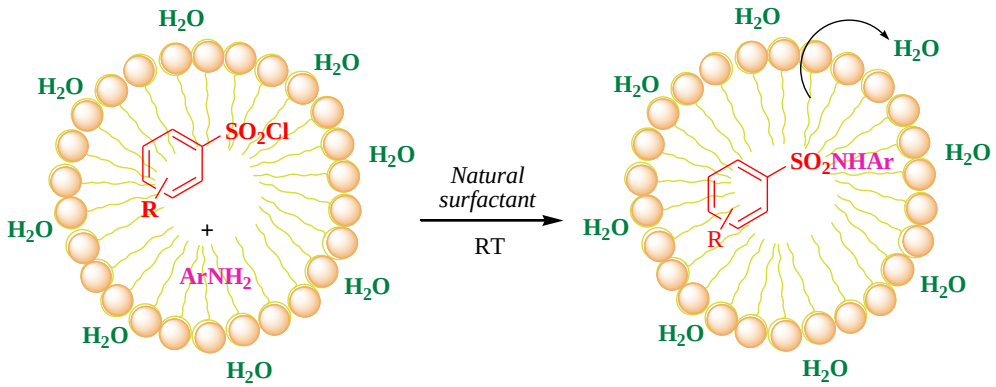
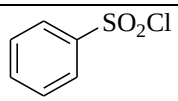
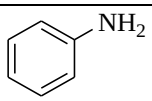
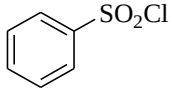
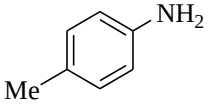
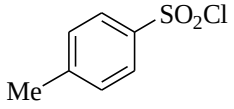
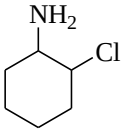
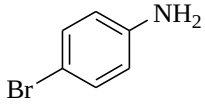
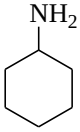
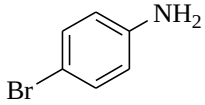
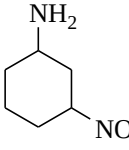
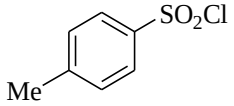
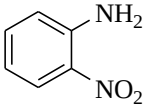
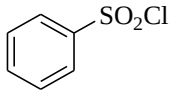
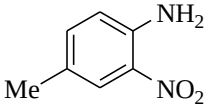
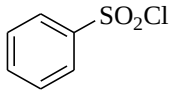
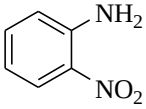
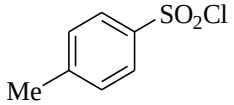
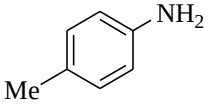
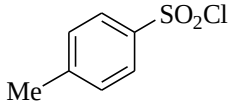
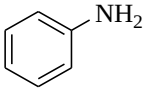
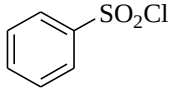
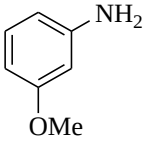


Figure 2. Micelle-promoted synthesis of sulfonamides

Table 2. Synthesis of sulfonamide derivatives (3a-k)

Entry	Sulfonyl chloride	Amine	Product	Time (hrs)	Yield (%)	M.P.(°C) Ref.
1.			**3a**	1.5	97	59-60[xlii]
2.			**3b**	1.2	92	118-119[xlii]
3.			**3c**	1.2	90	105-107[xliii]
4.			**3d**	1.5	88	100-102[xliii]
5.			**3e**	2.2	86	116-118[xliii]
6.			**3f**	2.2	92	112-113[xlii]
7.			**3g**	2.5	90	100-102[xlii]
8.			**3h**	2.5	96	101-103[xlii]
9.			**3i**	2.1	88	114-115[xlii]
10.			**3j**	1.5	90	95-97[xlii]
11.			**3k**	1.2	92	87-88[xliv]

CONCLUSION:

From the current methodology, we are able to describe an environmental friendly, efficient and economical catalyst for the synthesis of derivatives in aqueous extract of *Acacia concinna* pods medium. The application of biocatalyst in field of organic synthesis, water as medium, medium reaction condition and easy reaction workup are some of the advantages of present methodology.

EXPERIMENTAL SECTION:

General Remarks. All chemicals were obtained commercially from suppliers and were used without purification. Melting points were recorded on Digital Electro thermal Melting point apparatus and are uncorrected. Reaction monitoring was conducted using Thin Layer Chromatography (TLC) using pre-coated Silica gel 60 F_{254} plates with layer thickness 0.25nm purchased from Merck Ltd. TLC plates were visualized under ultraviolet light at 254 nm wavelength.

General procedure for the preparation of catalyst

A fine powder of *Acacia concinna* pods (20 g) in water (100 mL) was heated in a 250 mL conical flask at 100^{o}C for 20 min. The solid material was filtered and the aqueous extract was collected. The prepared extract has concentration 20% w/v.

General procedure for the synthesis of sulfonamide derivatives

A mixture of aromatic sulfonyl chloride (1mmol), and amine (1 mmol) in catalyst solution (20%, 10 mL) was stirred at room temperature for specified time (Table 2). After completion of the reaction (as indicated by TLC), a separated solid was filtered on Buchner funnel, washed with water and dried to obtain pure products in excellent yields.

Spectral data of representative compounds:

Phenyl(phenylsulfonyl)amine (3a)- White solid; Yield 80 %; mp: 59-60 ^{0}C;
^{1}HNMR (400MHz, DMSO-d^{6}): δ 4.39 (1H, bs, -NH), 7.01-7.02 (1H, d, Ar-H), 7.06-7.08 (2H, d, Ar-H), 7.19-7.23 (2H, m, Ar-H), 7.53-7.55 (2H, d, Ar-H), 7.58-7.59 (1H, d, Ar-H),7.73-7.75 (2H, d, Ar-H). **LCMS (ESI):** m/z 233

(4-Methylphenyl)(phenylsulfonyl)amine (3b)- White solid; Yield 80 %; mp: 118-119 ^{0}C;
^{1}H NMR (400MHz, DMSO-d^{6}): δ 2.17 (3H, s, CH_3), 4.57 (1H, bs, -NH), 6.94-6.96 (1H, d, Ar-H), 7.00-7.02 (1H, d, Ar-H), 7.50-7.60 (2H, m, Ar-H), 7.70-7.72 (1H, d, Ar-H). **LCMS (ESI):** m/z 247

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