

Isolation and structural studies on new natural products of potential biological importance

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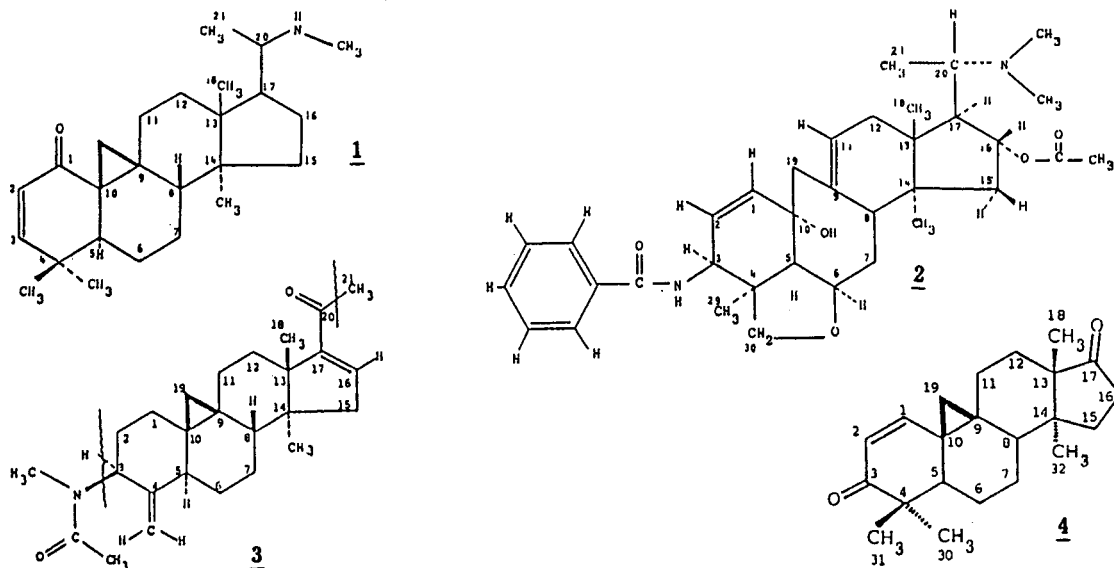
Abstract:-A number of new natural products have been isolated from indigenous medicinal plants as well as from marine plants and animals. These include indole alkaloids, steroidal alkaloids, sesquiterpenes, diterpenes saponins etc. The structures of these compounds have been elucidated with the help of modern spectroscopic techniques such as mass spectroscopy (E.I., C.I., F.D., +Ve FAB, -Ve FAB etc.) and 2D NMR spectroscopy (2D J-resolved, COSY-45,^o NOSEY, DEPT, hetero, COSY, Long range heterocosity, INADEQUATE, etc.). The structures have been confirmed in a few compounds by X-ray crystallography.

INTRODUCTION

Large sections of populations living in rural areas of the Afro-Asian countries rely on the indigenous medicinal systems for the treatment of diseases. These are largely based on the use of roots, leaves, fruits and flowers of different plant materials. Isolation, structural and synthetic studies have accordingly been directed to the discovery of new natural products in many laboratories, including ours. Our interest is however not limited to traditional medicinal plants but we also pay attention to any new leads encountered in other natural sources. For instance marine plants and animals are an invaluable source of novel secondary metabolites many which possess a wide diversity of structures and pharmacological properties which match those obtained from terrestrial organisms. Some of the recent studies carried out by us are briefly presented here.

CHEMICAL CONSTITUENTS OF *Buxus papilosa*

Buxus papilosa (Buxaceae) is a shrub, widely distributed in the northern regions of Pakistan. This plant is a potential source of steroidal alkaloids. We have previously isolated over 40 new steroidal alkaloids from its leaves. The new alkaloids recently isolated are cyclobuxoviramine (1), buxafuranamide (2) (a novel alkaloid having an ether linkage between rings A and B of the steroidal base) and (+)-*N*-acetyl-*N*-demethylcyclomicrobuxeine (3). Temperature dependent ¹H-NMR studies on (3) indicate that it exists as a mixture of two conformers which equilibrate at higher temperatures. A new triterpenoid, buxatenone, has also been isolated from the roots of this plant. Buxatenone is structurally related to cyclobuxoviracine, an alkaloid reported by us previously (ref 1).



NEW BISINDOLE ALKALOIDS FROM *Petchia ceylanica*

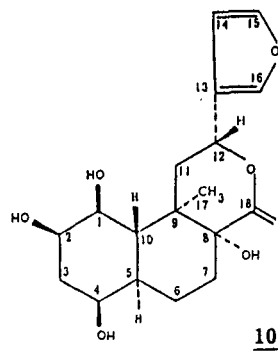
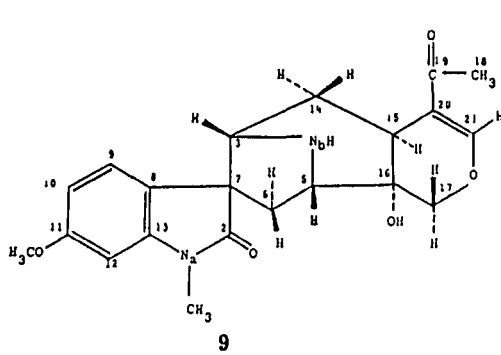
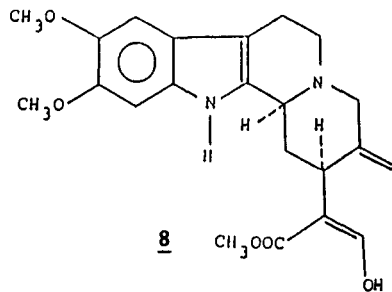
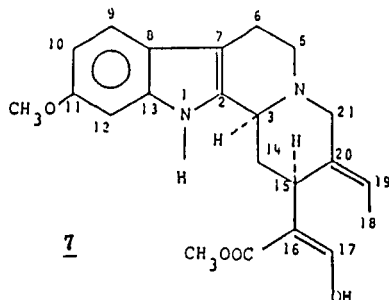
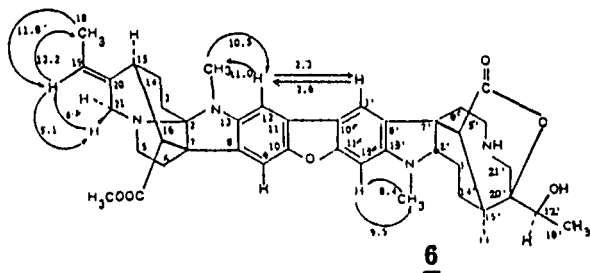
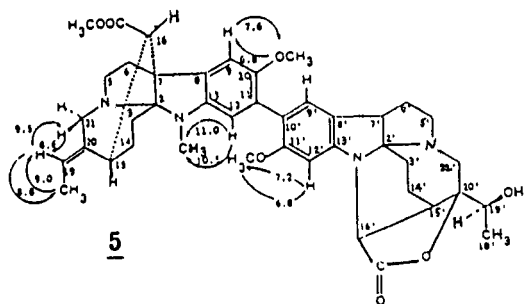
Petchia ceylanica (Apocynaceae) is a plant found in the lowlands of Sri Lanka. A number of bisindole alkaloids having vincorine-type moieties linked together have been previously reported by us from this plant. As a result of further isolation and structural studies, two new bisindole alkaloids, ceylanine (5) and ceylanicine (6), have now been isolated. Ceylanine (5) represents the first bisindole alkaloid have a vincorine-type unit linked to a pleiocarpamine skeleton, through a bond between the benzene rings of the two moieties.

NEW ALKALOIDS FROM *Alstonia macrophylla*

Alstonia macrophylla Wall is a common plant in Sri Lanka. It is a rich source of monomeric and dimeric indole alkaloids. We have isolated three new alkaloids from this plant: 11-methoxygeissoschizine (7), 10,11-dimethoxygeissoschizine (8) and 16-hydroxy-N₁₀-demethylalstophylline (9). Geissoschizine is a key intermediate in the biosynthesis of indole alkaloids.

A NEW DITERPENE FROM *Tinospora malabarica*

Tinospora malabarica (Miers) is cultivated throughout Pakistan. A novel furanoid bisnorditerpene, malabarolide (10), has been isolated from the fresh stems of this plant and its structure confirmed using X-ray crystallography and spectroscopic techniques. A number of 19-nor-clerodanes (ref. 2) have been reported previously, but malabarolide represents the first example of a 18,19-bisnorclerodane. A plausible biogenesis of malabarolide would involve oxidative removal of the 18-methyl group from a 19-norclerodane, or decarboxylation of a tinophyllol-type compound.



NEW ALKALOIDS FROM *Rhazya stricta*

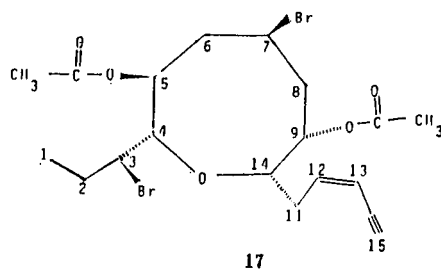
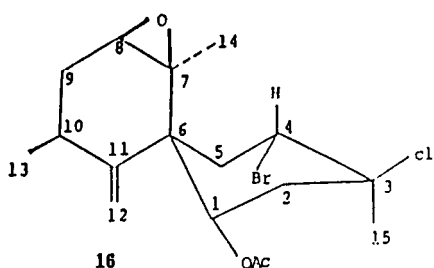
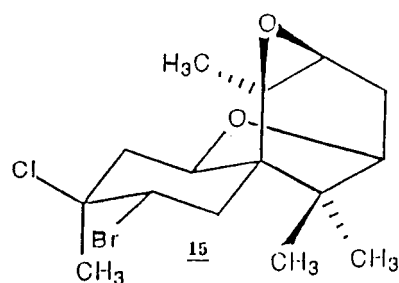
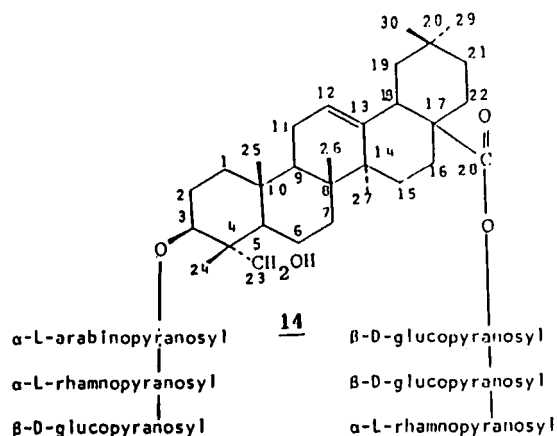
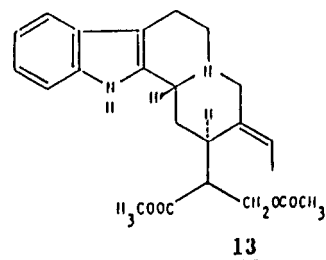
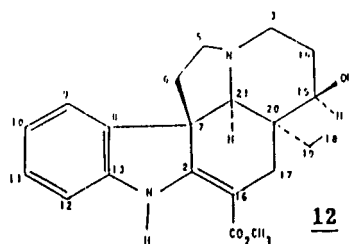
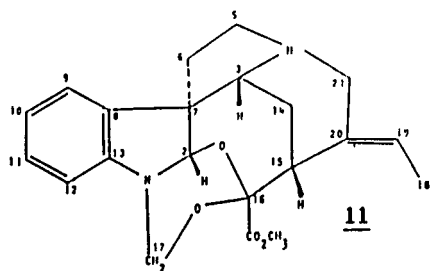
Rhazya stricta Decaisne (Apocynaceae) is a small shrub, growing profusely near Karachi. It is used in the indigenous system of medicine as a bitter tonic, for soar throat and in fever. We have previously reported twenty new alkaloids from it (ref.3). Recently we have isolated three new indole alkaloids rhazizine (11), 15-hydroxyvincadiformine (12) and bhimberine acetate (13).

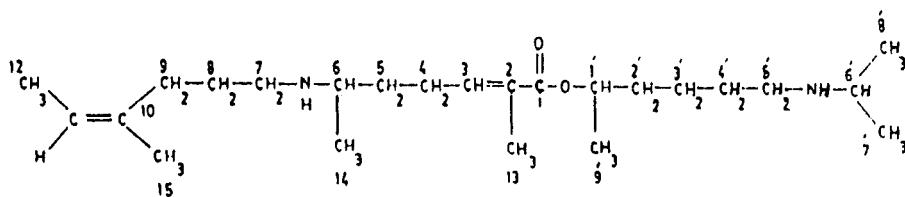
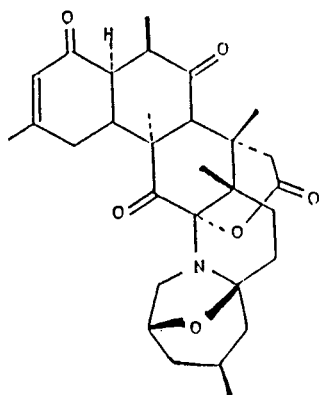
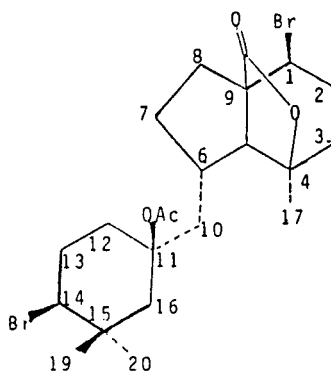
A NEW SAPONIN FROM *Nigella sativa*

Nigella sativa Linn (Ranunculaceae) is an indigenous herbaceous plant. We have previously reported a number of alkaloids from it (ref.4). Recent studies on the chemical constituents of the seeds of this plant have led to the isolation of a new triterpenoidal saponin nigelloside, (14). The structure of this saponin has been elucidated through spectroscopic studies and by chemical degradation.

CHEMICAL CONSTITUENTS OF *Laurencia pinnatifida*

As a result of our studies on chemical constituents of marine plants and animals in the intertidal zone near Karachi, we have investigated red and brown algae and various marine animals. *Laurencia pinnatifida* belongs to the family Rhodomalaceae. *Laurencia* species are well known for the halogenated compounds of varied chemical structures and diverse biological properties such as antimicrobial activity, cytotoxicity etc. We have isolated pinnatazane (15), a new bridged sesquiterpene from *Laurencia pinnatifida* and its structure has been established through spectroscopic and X-ray crystallographic techniques. Another sesquiterpene, pinnatinate (16) has also been isolated from this alga which is an acetylated product of a previously known chamigrine alcohol (ref.5) Along with these sesquiterpenoids a new non-isoprenoid acetylenic cyclic ether, pinnatifidine (17) has been isolated which represents the first diacetylated dibromo representative of this class.



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A NEW LINEAR METABOLITE FROM *Stockeyia indica*

Stockeyia indica is a brown marine benthic alga, occurring in mid to lower littoral pools. A novel linear metabolite (18) has been isolated and its structure has been established with the help of modern spectroscopic techniques.

NEW ALKALOID FROM ZOANTHID SPECIES

Zoanthids are small marine animals found growing as dense mats on intertidal rocks. From an unidentified species of zoanthid we have isolated a new alkaloid zoanthaminone (19) which belongs to a new class of alkaloids.

A NEW DITERPENOIDAL LACTONE FROM *Aplysia juliana*

Aplysia juliana (sea hare) is a marine animal, belonging to the class of opisthobranch molluscs. During the course of our studies on the chemical constituents of *Aplysia juliana* we have isolated a new diterpenoidal lactone, agnasyl acetate (20).

Many of the compounds reported above have shown interesting anti-bacterial, anti-viral and anti-cancer activities.

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