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A REVIEW ON PHARMACOLOGICAL ACTIVITIES OF *HIPPOPHAE RHAMNOIDES*

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ABSTRACT

Dependence on natural medicines in the administration of illnesses is still a lot of experienced by a huge portion of the individual particularly rustic inhabitants because of their simple availability and cost viability. Sea buckthorn (*Hippophaerhamnoides L.*) belongs to family Elaeagnaceae, a one of important plant basically for its therapeutic and nourishing potential. Sea buckthorn (SBT) is a prickly nitrogen-fixing deciduous bush of cold dry climate confined to Europe and Asia. It is at present tamed in a few portions of the world because of its nourishing and therapeutic properties. The entire plant of sea buckthorn and particularly its berries are a wellspring of countless distinctive bioactive mixes. The best consideration has been attracted to its high substance of nutrients, minerals, common cancer prevention agents and proteins. Sea buckthorn is esteemed for its cardio protective, anti-atherogenic, anti-diabetic, hepatoprotective, hostile to cancer-causing, immunomodulatory, antioxidant, antiviral, antibacterial, mitigating and vasorelaxant impacts. This review sums up the pharmacological activities of *Hippophaerhamnoides*.

Keywords: *Hippophaerhamnoides,* pharmacological activities and medicinal herb.

INTRODUCTION

Medicinal plants turned out to be an integral part of human progress to battle sicknesses from the earliest starting point of humankind. Medicinal plants can be a significant wellspring of recently known synthetics, with conceivable helpful impacts. Customary practice is the therapeutic utilization of plants, a lot more established than regular pharmaceutical, pharmacological, and substance sciences. The world association has assessed that for its fundamental medicinal service needs; in excess of seventy five percent of the world's population already relies upon plant-inferred drugs, normally got from conventional healers. Due to their broad biological and therapeutic practices, natural drugs are popular for essential social insurance in developed as well as underdeveloped nations. The utilization of plants as a wellspring of prescriptions for the fix of numerous infections returns to ancient times and individuals from all continents have this old practice. The medicinal properties of therapeutic plants are expected to a great extent to the presence of various complexes synthetic compositional intensifies that exist as secondary metabolites. Which are characterized into flavonoids, alkaloids, saponins, glycosides, starches, tannins and basic oils.

The word *Hippophae* has originated from a Latin word 'Hippo' which means pony and

'Phaos' which signifies 'sparkles' [1]. *Hippophaerhamnoides* has a place with family Elaeagnaceae usually known as Sea buckhorn (SBT) [2]. It is a group of eudicots of the Rosales order. The family incorporates around 100 species in three genera for the most part found in the moderate geological scopes of the Northern side of the equator. Sea berries are grouped in the plant scientific classification into six species and 12 subspecies [3]. Seaberries developed in the Czech Republic for the most part incorporate sea buckthorn and Russian silverberry. *Hippophaerhamnoides* is a deciduous, dioecious plant with various greenish-yellow blossoms and brilliant orange, globular, ellipsoid natural product. It is local to Europe, India, Nepal, Bhutan, Pakistan, France, Afghanistan, Myanmar, Finland, Romania, Germany, Russia and Britain [4]. In india, *Hippophaerhamnoides* is broadly dispersed in chilly Himalayan district at a height of 2500-4000m [2]. *Hippophaerhamnoides* bush is 2 meter tall with 2-6 cm long leaves. It is well developed all around in depleted soil with pH 5.5-8.3. *Hippophaerhamnoides* plant can persevere through aextraordinary temperature of 40-43ºC [4].

The entire plant of *Hippophaerhamnoides* is significant, berries are the most significant part from which the juice is removed [4]. *Hippophaerhamnoides* juice is a significant wellspring of some important synthetic substances, for example, tocopherolmcrotrients, organic acids, vitamin C and polyunsaturated fatty acids. The juice of *Hippophaerhamnoides* was the regular medication utilized in antiquated. The berries (fruits) of *Hippophaerhamnoides* are maturated in three stages. The first stage is the quickening seed development, second stage is the declining progress seed development and the last third stage is the known as berry development stage. In most region of the world including Pakistan the berries are aged toward the beginning of September. In the event that the branches are not upset, at that point the berries stay entire of the winter connected to the branches [5]. The natural products are known to be a rich wellspring of nutrients, carotenoids, flavonoids and sugar alcohols. The leaves contain a wonderful amount of supplements and bioactive substances, for the most phenolic part. It was additionally detailed that *Hippophaerhamnoides* leaf has no cytotoxicity or unfavourable impact after oral organization [2]. The leaves and organic products have been utilized as germicide and twisted mending just as in the treatment of ulcers in people asmedications in Turkey [6]. Sea buckthorn seed can be utilized as oil and the leaves to make tea. While tea produced using the seeds have diuretic properties and help in weight reduction, imbuements of the leaves have antidiarrheal properties; also, organic product teas reinforce the safe framework, and show action against skin problems. The positive and special properties of sea buckthorn have been known since VII Century BC. The plant was utilized in characteristic medication, yet in addition, in veterinary medication as a methods for soothing helminthiasis in ponies and giving them progressively mass and a delightful, glossy coat. Now it is utilized in numerous businesses, particularly the pharmaceutical, corrective, and food ventures, yet additionally as an ornamental component, as firewood, or even as an apparatus for the restoration of ruined territories [7]. As per authentic records, sea buckthorn was first utilized as a medication in China, and in increasingly current occasions, the plant was officially recorded in the Chinese Pharmacopeia in 1977 [7]. From 5 decades, *Hippophaerhamnoides* has been utilized for the treatment of harms caused by radiations, swelling and burns in Chinese traditional medications[8]. *Hippophaerhamnoides* oils have been utilized in natruceuticals, regular prescriptions and beauty care products as crude materials in Russia for certain decades [9]. *Hippophaerhamnoides* oil have additionally been utilized in the treatment of skin issue, for example, dermatitis, psoriasis, lupus erythematosus and dermatosus[10]. *Hippophaerhamnoides* has been utilized in different areas of the world as customary medication for the treatment of acid reflux, hack and blood sepsis [11].

At present, sea buckthorn has become well known particularly for its constructive outcomes on the human living being. It likewise diminishes stomach ulcers, underpins wound mending, quickens treatment of skin issue and lessens torment [12-14]. Sea buckthorn acts against asthma and aspiratory ailments [15], against expanded sebum emission and influences platelet

accumulation[4]. Its antistress and adaptogenic exercises have been affirmed [14]. Sea buckthorn likewise emphatically influences metabolic ailments [3], with the capacity to hinder maturing and ensure against radiation-actuated harm, quicken the recuperating of consumes and frostbites, and lessen balding. Sea buckthorn likewise influences mental capacities, specifically diminishing memory misfortune in old individuals. Its beneficial outcomes have been used for quickening of wound recovering, particularly in individuals after ear, nose and throat tasks where sea berry oil has been a part of the treatment. The oil has been utilized for insurance against sun based radiation [16]. Sea berry items might be utilized in different medication structures from fluids through powder, pastes, patches, films, treatments and mist concentrates to suppositories [16]. *Hippophaerhamnoides* plant has impervious to dry season, cold, and soluble base and salt. The perplexing root framework with nitrogen-fixing of the *Hippophaerhamnoides* an ideal pioneer plant in soil and water protection zone [9]. Sea buckthorn is a wellspring of natural acids, basically malic acid, quinicacid, oxalic acid, oleic acid, citrus acid, and tartaric acid. Sea buckthorn is a decent wellspring of flavonoids as well, fundamentally quercetin, kaempferol, myricetin, and isorhamnetin, and a significant wellspring of tocopherols[17].Phytochemical examination of the plant affirmed the nearness of mineral acids, carotenes, flavonoids, nutrients, sugars and amino acids [18]. Sea buckthorn is esteemed for its cancer prevention agent, cardioprotective, antiatherogenic, antidiabetic, hepatoprotective, hostile to cancer-causing, immunomodulating, antiviral, antibacterial, mitigating and vasodilating impacts. Other significant properties of sea buckthorn incorporate its cytoprotective impacts.

PHARMACOLOGICAL ACTIVITIES OF *HIPPOPHAE RHAMNOIDES*

Examination on restorative plants is expanding step by step. *Hippophaerhamnoides* is an enchantment plant as it contains a biodiversity of both dietary just as therapeutic constituents. This review discussed the pharmacological activities of *Hippophaerhamnoides*.

Antioxidant Activity

The antioxidant activity of *Hippophaerhamnooides* was determined by two techniques at different concentrations ranging from 0.0625-0.5mg/ml. One is DPPH technique in which butylatedhydroxytoulene (BHT) was used as reference standard and second one is ABTS technique in which trolox was used as a reference standard. IC_{50} values of both techniques were obtained. IC_{50} estimation of fluid concentrate was seen as essentially lower than BHT utilized in DPPH technique, while IC_{50} esteem by ABTS technique couldn't be determined as concentrate showed very low antioxidant activity. IC_{50} estimations of MeOH remove acquired by DPPH and ABTS technique were seen as fundamentally equivalent to the IC50 estimations of the particular reference guidelines (BHT and Trolox). This recommended MeOH leaf extract have antioxidant activity and is more dynamic than watery concentrate [19].

In-vitro investigation of hydrophilic concentrate of *Hippophaerhamnoides* indicated great antioxidant activity, which was like the antioxidant activity of the methanolic concentrate of *Hippophaerhamnoides*[20]. The antioxidant activity of *Hippophaerhamnoides* might be because of its higher phenolic and flavonoids substance [8]. *Hippophaerhamnoides* gives a superb wellspring of basic unsaturated fats that is 70% of its composition. The seed oil is utilized as hostile to maturing, antioxidant, anti-inflammatory and as regular UV blocking operator in restorative plans. The inhibitory impacts of alcoholic leaf and organic product concentrate of *Hippophaerhamnoides* have been examined to repress the oxidative harm instigated by chromium. Alcoholic leaf and natural product remove were found to forestall chromium initiated free extreme creation and reestablished the antioxidants status. It has been indicated that product of *Hippophaerhamnoides* restrain nicotine instigated oxidative pressure. It has been exhibited by different in-vivo, in-vitro contemplates that *Hippophaerhamnoides* has antioxidants activity [10].

Antibacterial Activity

Antibacterial activity of *Hippophaerhamnoides* leaf removes

alongside antibiotic medication utilized as standard was assessed against Escherichia coli (MTCC 739), Arthobacterprotophormial (MTCC 2682) and Micrococcus luteus (MTCC 106). Affectability of various bacterial strains to *Hippophae* was estimated as far as zone of hindrance utilizing agar-well dispersion test strategy and paper plate dissemination technique. The *Hippophaerhamnoides* methanolic leaf extract showed wide range against human pathogens. The *Hippophaerhamnoides* methanolic leaf was discovered best against E. coli in which a most extreme zone of restraint (24mm) was seen at a convergence of 25 mg mL-1 while hindrance for (8mm) for M. luteus[2]. Michel et al. [12]gave detailed antibacterial activity of *Hippophaerhamnoides* using distinctive concentrate against *Staphylococcus aureus*. The current investigation demonstrated that 6mg/ml of both the n-hexane and chloroform concentrates of *Hippophaerhamnoides* berries and 6mg/ml of n-hexane concentrate of leaves of the plant altogether ($p<0.05$) hindered the development of methicillin-safe *Staphylococcus aureus*. Antibacterial activity against*Staphylococcus aureus* was appeared by the various concentrates that was non-noteworthy ($p>0.05$). This antibacterial action might be huge at higher dosages, that estimation is just conceivable by disengaging the dynamic constituents. The n-hexane concentrate of leaves of the plant have antibacterial action against methicillin-safe Staphylococcus aureus (MRSA) [14].

Anti-inflammatory and immunomodulatory Activity

The SBT leaf separate was found to have critical calming action in adjuvant incited joint inflammation (AIA) rodent model and lipopolysaccharide actuated provocative reaction in murine macrophages [12]. In another investigation, disengaged casuarinin from the SBT leaves was investigated for the impact on the TNF- -initiated ICAM-1(intra cellular cell adhesion molecule) articulation in a human keratinocytes cell line. Pre-treatment with casuarinin restrained TNF- -actuated protein and mRNA articulation of ICAM-1 and ensuring monocyte adhesiveness in HaCaT cells. Casuarinin altogether restrained TNF- - actuated enactment of NF-B, ERK and p38 MAPK in a subordinate way. Pretreatment with casuarinin diminished TNF- - actuated ace provocative middle people, for example, IL-1, IL-6, IL-8, and MP-1. Further, in the murine macrophage cell line, SBT leaf alcoholic concentrate altogether repressed the upgraded creation of NO prompted by LPS (lipopolysaccharide) in a subordinate way and by its inhibitory impact on iNOS stimulation. As of late, SBT leaf alcoholic concentrate have appeared directed antigen introduction capacity of macrophages in matured mice, which showed its resistant boosting and hostile to maturing impact. Sea buckthorn berries additionally indicated immunoprotective impact against T-2 poison initiated immunodepression in 15-day-old chicks. SBT has been broadly utilized in oriental customary drugs for treatment of numerous incendiary issues. Henceforth from these perceptions, the mitigating and immunomodulatory exercises have been deductively demonstrated [12].

Anticancer Activity

In an investigation on MDA-MB-231 human bosom malignancy cells, Sea buckthorn procyanidins disconnected from the seeds have inhibitory effects on fatty acid synthase (FAS): a key compound for all over again long-chain unsaturated fat biosynthesis, significant levels of which are found in malignant growth cells. This restraint was portion subordinate at fixations running from 0 to 0.14µg/ml. A grouping of 0.087µg/ml repressed half of FAS action. In addition, cell development was smothered by treatment with sea buckthorn procyanidins at focuses somewhere in the range of 10 and 60µg/ml. Likewise, the tried procyanidins were found to initiate cell apoptosis in a portion subordinate way. The creators propose that these procyanidins can actuate MDA-MB-231 cell apoptosis by hindering intracellular FAS action [7].

Olsson et al. [21] looked at the effect of 10 different concentrates of foods grown from the ground, including sea buckthorn berries, on the multiplication of HT29 semi-colon malignant growth cells and MCF-7 breast cancer cells. They saw that sea buckthorn had the most noteworthy hindrance effect for the multiplication of HT29 and MCF-7 cells at its two most noteworthy directed focuses (0.25 and 0.5%). The creators propose that

the hindrance of malignancy cell multiplication was corresponded with convergences of carotenoids and vitamin C. Boivin et al.[22] decided the antiproliferative action of the juices of 13 sorts of berries, including ocean buckthorn, at centralizations of 10–50µg/ml against five disease cell lines in vitro: AGS—stomach adenocarcinoma, ACF-7—mammary organ adenocarcinoma, PC-3—prostatic adenocarcinoma, Caco2—colorectal adenocarcinoma, and MDA-MB-231—mammary organ adenocarcinoma. It was discovered that sea buckthorn berry juice, similar to blackberry and dark chokeberry juices, had antiproliferative properties. In any case, no connection was found between the counter proliferative properties of the berry juices and their cancer prevention agent limit, and the hindrance of malignant growth cell expansion by the juices didn't include caspase-subordinate apoptosis. In spite of this, concealment of tumor necrosis factor (TNF)-instigated initiation of nuclear factor kappa-light-chain enhancer of activated B cells (NFκB) was examined. The anticancer activity of sea buckthorn organic products might be founded on its improvement of the DNA- binding action of interferon regulatory factor-1 (IRF-1), a known antioncogenic interpretation factor causing development concealment and apoptosis.

Ant diabetic Activity

Ant diabetic movement was estimated by alpha-glucosidase inhibitor measure at various centralizations of the example running from 0.0625 to 0.50 mg/ml. Fluid leaf separate demonstrated low alpha glucosidase hindrance movement, that is, under half even at the most elevated fixation (0.50 mg/ml) taken in the investigation and hence IC_{50} value couldn't be resolved. MeOH leaf separate showed better antidiabetic action with 73.67% compound hindrance at 0.50 mg/ml fixation and IC50 esteem was seen as 0.25 mg/ml. This mirrored methanolic concentrate of sea buckthorn leaves contains certain compound(s) with alpha glucosidase inhibitory movement [19].

Anti-tumor Activity

The antitumor activity of sea buckthorn can be ascribed to antioxidant mixes, especially phenolic mixes, for example, flavonoids, including kaempferol, quercetin, and isorhamnetin; these shield cells from oxidative harm that can prompt hereditary change and to malignancy [13]. The current examination was attempted to survey the counter tumor movement of isorhamnetin secluded from *H. rhamnoides L*., utilizing hepatocellular carcinoma cells (BEL-7402). We found that the cytotoxic impacts of isorhamnetin demonstrated portion and time-reliance against BEL-7402 cells. We utilized the MTT [3-(4, 5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide] test to test the cytotoxic impacts of isorhamnetin, and found that isorhamnetin displayed powerful cytotoxicity against BEL-7402 cells, with IC_{50} equivalent to 74.4±1.13gml−1 for brooding 72h. Specifically, we found that the greater part of the BEL-7402 cells were disconnected from the outside of culture dish and were drifting in the medium after treatment with generally high centralization of isorhamnetin. Moreover, cytotoxicity of the flavonols on tumor cells relies upon cell collection of the medications. The measure of isorhamnetin gathered in BEL-7402 was examined by high-performance liquid chromatography (HPLC) and indicated that isorhamnetin could saturate the cell film into the cell. The estimation of isorhamnetin amassed in cells is little [23]. Zhang et al. [24] exhibited that infusion of seed oil (1.59 g/kg body weight) significantly repressed the development pace of transplanted melanoma (B16) and sarcoma (S180) tumors in mice.

Wound-Healing Activity

The defensive and therapeutic impacts of SBT against wounds, consumes, singes, ulcers and mucosal wounds have been broadly examined utilizing distinctive creature models and by clinical preliminaries. In the ongoing years, SBT leaf extricate has been experimentally explored and indicated that it improves intense and constant dermal injury mending (consumes and diabetic) in rodents. The SBT rewarded creature demonstrated quicker decrease in twisted region in correlation with control and silver sulfadiazine (standard consideration) rewarded creatures. The effective use of SBT expanded neovascularization, collagen blend and adjustment at twisted site, as prove by up-controlled articulation of vascular endothelial

development factor, collagen type-III, network metalloproteinases (MMP-2, 9) and expanded substance of hydroxyproline and hexosamine. SBT treatment likewise expanded the endogenous enzymatic and nonenzymatic antioxidant and diminishing in lipid peroxide levels in wound granulation tissue. Further, it has been accounted for that SBT leaf has no cytotoxic, overwhelming metal defilement and antagonistic impact after oral organization. Flavonoids are one of the significant naturally dynamic substances present in SBT leaves and organic products. The positive mending impact of effective utilization of SBT flavone (segregated from organic product mash) (1.0%, w/v) has been seen on dermal injuries in test rodents [12].

Hepatoprotective Activity

The liver is regularly influenced by a large number of natural contaminations and medications, all of which place a weight on this crucial organ that can harm and debilitate the liver and in the end lead to hepatitis or cirrhosis. The hepatoprotective action of SBT leaves and seed oil was assessed utilizing carbon tetrachloride (CCl_4) instigated hepatic harm in creatures, and the outcomes indicated that both SBT leaf alcoholic concentrate and seed oil enhanced CCl_4-actuated liver injury as confirm by both histological and biochemical discoveries. In an ongoing report by Maheshwari et al. [25], a portion of the phenolic constituents of leaves, for example, gallicacid, myricetin, quercetin, kaempferol and isorhamnetin were distinguished in the phenol rich part (PRF) by reverse phase high performance liquid chromatography (RP-HPLC). Oral organization of PRF at portion of 25–75 mg/kg BW fundamentally shielded from CCl_4 initiated height in aspartate aminotransferase, alanine aminotransferase, - glutamyltranspeptidase and bilirubin in serum, upgraded the hepatic antioxidants. These perceptions propose that PRF has intense antioxidantaction and ensured against CCl_4 prompted oxidative harm in the liver. Be that as it may, increasingly precise investigations on interminable liver injury ought to be done for the advancement of an item or a plan. SBT might be a cheerful medication for avoidance and treatment of liver fibrosis, yet further all around controlled clinical preliminaries are required.

Anti-stress and adaptogenic Activity

The natural details which can improve physical perseverance, mental capacity and vague opposition of the body to pressure have been named as adaptogen. The adaptogenic movement of SBT leaf extricates was concentrated in rodents utilizing a latent cold (5 ℃) hypoxia (428 mmHg) restraint (CHR) creature model. SBT leaf fluid concentrate controlled orally in rodents at a portion of 100 mg/kg BW both in single and five dosages 30 min before CHR introduction had huge enemy of stress and adaptogenic action. The impact of the concentrate was concentrated on lipid peroxidation and cancer prevention agent boundaries in liver and gastrocnemius muscle of rodents. Results proposed that supplementation with SBT leaf extract decreased the oxidative worry in liver and muscle of rodents during CHR presentation and post-stress recuperation. During serious unpleasant introduction to CHR and post pressure recuperation the vigorous digestion just as hexose monophosphate pathway is stifled. The single and five dosages of SBT separate treatment confined the abatement or better kept up tissue glycogen and compound exercises for example hexokinase, phosphofructokinase, citrate synthase and glucose-6-phosphate dehydrogenase, in blood, liver and muscle, during CHR introduction. The examinations recommended that SBT leaf fluid concentrate treatment made a pattern for moving anaerobic digestion oxygen consuming during different pressure CHR presentation and post pressure recuperation [12].

Cardio protective and anti-atherogenic Activity

Healing impact of SBT arrangements on cardiovascular illnesses are known and all around reported in Tibetan customary clinical writing. A few investigations on human and creatures have been completed to assess the impact of flavonoids of SBT on cardiovascular sicknesses, as some flavonoid mixes are known to have positive ionotropic impacts. Flavonoids in SBT foods grown from the ground are notable to improve the working of cardiovascular framework. The total flavonoids of *Hippophae* (THF), extricated from its leaves and organic

product, is a gathering of mixes containing seven sorts of flavonoids. Among them, the principle segments are isorhamnetin and quercetin. THF treatment displayed defensive impacts on myocardial ischemia and reperfusion, tumors, oxidative injury and maturing [12]. The investigation by Pang et al. [26] exhibited the antihypertensive impact of absolute flavones extricated from seed buildups of SBT in ceaseless sucrose took care of rodents by controlling its insulin and angiotensin II levels. The hypertension, hyperinsulinemia, dyslipidemia and actuated angiotensin II incited by the high-sucrose diet could be improved by absolute SBT flavones and the ideal impact was seen at the portion of 150 mg/kg/day. SBT supercritical CO_2-removed seed oil have been appeared to have hostile to atherogenic and cardioprotective exercises. In an investigation utilizing bunny as a creature model, organization of SBT seed oil alongside elevated cholesterol diet confined further ascent of absolute cholesterol and caused a noteworthy decay of triglyceride and (low density lipoprotein) LDL-cholesterol when contrasted with creatures benefited from elevated cholesterol diet as it were. The ascent in (high density lipoprotein) HDL-cholesterol over the basal qualities in seed oil rewarded creatures was altogether higher than the non-rewarded creatures. SBT seed oil additionally caused a huge vasorelaxation [27].

Anti-viral and antimicrobial Activity

A precise substance examination of dynamic divisions from the SBT leaves has prompted the revelation of another phytochemical medicate Hiporamin, having a wide range of antiviral and antimicrobial exercises. Hiporamin is a filtered portion of polyphenol division, containing monomeric hydrolysable gallo-ellagi-tannins. It was found to have a solid enemy of infection action and wide scope of activity against Influenza and Herpes infections. Antiviral movement of Hiporamin in regard of Influenza infection was seen by its inhibitory impact on the viral neuraminidase. It likewise demonstrated inhibitory impact in a HIV contamination in the cell culture and antimicrobial movement. The SBT leaf extract additionally has a noteworthy enemy of dengue action when assessed in Dengue infection type-2 tainted blood-determined human macrophages with a reduction and increment in TNF-and IFN-separately[12].

Fig. 1: Berries of *H. rhamnoides*

Fig. 2: Leaves of *H. rhamnoides*

CONCLUSION

Present study provides review about medicinal importance of *Hippophaerhamnoides.* All plant parts are useful in treating different diseases and ailments very effectively. Recent review also reveals many pharmacological activities of *Hippophaerhamnoides* like antibacterial, antiviral, adaptogenic, antistress, anti atherogenic, cardio protective, wound healing, hepatoprotective, anti-tumor, anti-diabetic, anti-cancer anti-inflammatory activities.

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