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Miraculous Role of Salicylic Acid in Plant and Animal System

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Abstract: This study briefly focuses on the diverse role of Salicylic Acid (SA) in humans, in curing different diseases and in plants, in ameliorating biotic and abiotic stresses. SA has also been implicated in several other processes in plants like thermogenesis, flowering, germination, fruit yield, bioproductivity, etc. SA functions as a protective agent both in animal and plant systems. Thus, SA could aptly be called a wonder compound.

Key words: Salicylic acid, biotic and abiotic stress

Introduction

Centuries ago, the Americans, Indians and ancient Greeks discovered that leaves and bark of the willow tree cured aches and fevers. Breakthrough came in 1828 when Johann Buchner, working in Munich, isolated a little amount of Salicin, the glucoside of Salicylic alcohol, which was the major Salicylate in willow bark. The use of willow tree bark to relieve pain in believed to be as old as the 4th century B.C., when Hippocrates prescribed it for women during child birth (Rainsford, 1984). The name Salicylic Acid (SA), from the latin word salix for willow tree, was given to this active ingredient of willow bark by Raffaele piria in 1838. The first commercial production of Synthetic SA began in Germany in 1874. Aspirin, a trade name for Acetyl Salicylic Acid (ASA), which produces less gastrointestinal irritation yet has similar medicinal properties, was introduced by the Bayer Company in 1890 and rapidly became one of World's best selling drugs (Raskin, 1992) (Fig. 1a). In spite of the fact that the mode of medicinal action of Salicylates is a subject of continual debate, they are being used to treat human diseases ranging from the common cold to heart attacks and in alleviating biotic and abiotic stress in plants.

Salicylic acid belongs to a diverse group of plant phenolics. These are compounds with an aromatic ring bearing a hydroxyl group or its functional derivative (Fig. 1b). The most important

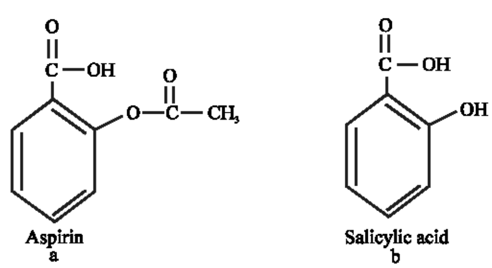

Fig. 1: Structure of aspirin (acetyle salicylic acid) and salicylic acid

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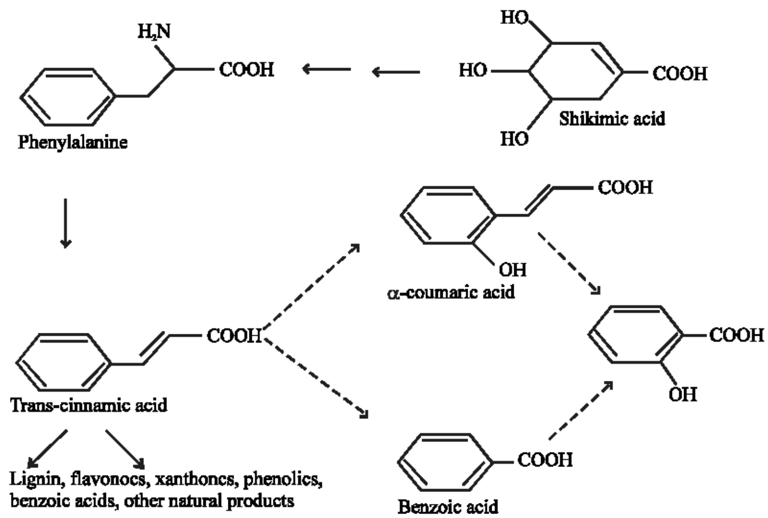

Fig. 2: Pathways of production of salicylic acid (Yalpani *et al*., 1993)

mechanism for formation of SA is the side chain degradation of cinnamic acids, which are important intermediates in the shikimic acid pathway. The conversion of cinnamic acid to SA probably proceed via benzoic or ortho-coumaric acid (Chadha and Brown, 1974) (Fig. 2).

Salicylic Acid and Human Health (Hughes, 2006)

The role of SA in treating human diseases is well known. Aspirin is the general name for acetyl salicylic acid (ASA), which undergoes spontaneous hydrolysis to SA in aqueous solutions and thus it is SA, which functions as an effector molecule. The synthetic drug was developed as an analgesic (pain killer) and this is still the main purpose of the drug in most people's minds. It was the first NSAID (Non steroidal anti-inflammatory drug) and probably still the most effective.

During the history, aspirin has been found to have a number of uses besides pain relief. Current uses of aspirin includes-

- Over-the-counter pain relief, especially for headaches
- Reduction of swelling and inflammation in arthritis and injuries.
- Anti-coagulant given to sufferers of heart attack, mini-stroke and unstable angina.
- Can reduce severity of heart attack if taken at first symptoms.
- Recovery after cardio-vascular surgery (e.g., by pass operation)
- Treatment of rheumatoid arthritis, osteoarthritis and other rheumatoid diseases.
- In controlling diabetes.

Possible benefits of aspirin are being researched in

- Migraine treatment
- Improving circulation in the gums
- Fighting ovarian, breast and colon cancer
- Prevention of cataract
- Controlling pre-eclampsia
- Improving brain function, especially memory

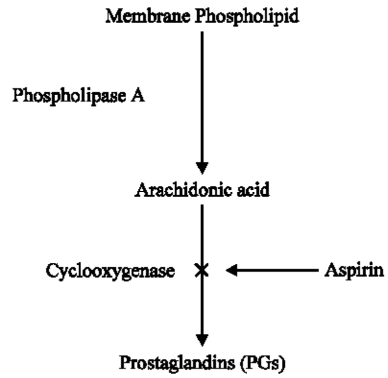

Fig. 3: Inhibition of cyclooxygenase (COX) by Aspirin. Prostaglandins (PGs) are produced from the conversion of membrane phospholipid into Arachidonic acid by an enzyme phospholipase A. Cyclooxygenases then convert Arachidonic acid into prostaglandins

- Reducing colorectal cancer repeating
- Prevention of adult leukemia
- Prevention of HIV replicating
- Reduce prostrate cancer risks
- Increasing success rates of IVF programs

Mechanism of Action

When we are injured, our body produces prostaglandins, which are complex fatty acids that act like hormones within body tissues. Prostaglandins act by stimulating the dilation of blood vessels and muscle contraction and this results in pain.

Prostagladins are produced from the conversion of membrane phospholipid into arachidonic acid by an enzyme phospholipase A. Arachidonic acid is then converted into prostaglandins by cyclooxygenase enzyme. Aspirin appears to stop the production of prostaglandins by inhibiting cycloxygensase (Fig. 3).

Salicylic Acid Ameliorates Biotic Stress

Biotic stress is a biological insult (e.g., insects, diseases) to which a plant may be exposed during its lifetime. SA is widely distributed in monocot and dicot plants (Cleland and Ajami, 1974; Baardseth and Russwurm, 1978; Swain *et al*., 1985; Raskin *et al*., 1990). While the healing properties of plants containing high levels of SA have been known since antiquity, the first insights regarding SA's role in plants have emerged only during the past decade. Vertebrate animals possess a novel and highly specific immune system that acts as a defense against diseases. Plants react to pathogen attack by activating elaborate defense mechanisms, which are less understood than the Vertebrate immune system. These defense mechanisms are activated both at the site of infection and at distal uninfected parts of the plant leading to necrosis or Hypersensitive Response (HR) and Systemic Acquired Resistance (SAR), respectively. An extensive body of research tells that SA ameliorates biotic stress in plants. When a plant is infected with a pathogen to which it is resistant, a wide variety of biochemical and physiological responses are induced. Many of these responses are believed to protect by restricting, or eliminating the pathogen and by limiting the damage it causes. In contrast when a plant is infected with a pathogen to which it is susceptible, the pathogen replicates and frequently spreads throughout the plant, causing extensive damage and even death of the host.

The first evidence that SA might be involved in plant defense was provided by White (1979), which found that injection of Aspirin or SA into to tobacco leaves enhanced resistance to subsequent infection by Tobacco Mosaic Virus (TMV). This treatment also induced Pathogenesis-related proteins (PR proteins) accumulation (Antoniw and White, 1980). Most of the PR proteins have been shown to have antimicrobial activity *in vitro* or the ability to enhance disease resistance when over expressed in transgenic plants (Weete, 1992; Malamy and Klessig, 1992). In addition to enhancing resistance to TMV in tobacco, SA also induced resistance against many other narcotizing or systemic viral, bacterial and fungal pathogens in a variety of plants (Weete, 1992; Malamy and Klessig, 1992). SA was also found to induce PR proteins in a wide range of both dicotyledonous and monocotyledonous plants including tomato and *Gomphrena globosa* (White *et al*., 1987), potato (Hooftvan *et al*., 1986), bean (Metraux *et al*., 1989), cowpea (Hooftvan *et al*., 1986; Metraux *et al*., 1989), cucumber (Matsuta *et al*., 1991), rice (Simmons *et al*., 1992), garlic (Van Damme *et al*., 1993), soybean (Crowell *et al*., 1992), azukibean (Ishige *et al*., 1992), sugarbeet (Flemming *et al*., 1991) and *Arabiopsis thaliana* (Uknes *et al*., 1992).

Salicylic Acid Ameliorates Abiotic Stress

Abiotic stress is a physical (e.g., light, temperature) or chemical insult (e.g., Salt pollutants) that the environment may impose on a plant. The crops growing under stress conditions suffer loss in yield, the magnitude of which depends on the severity of stress as well as inbuilt genetic and biochemical make up of the individual plant. A decrease in fresh weight, dry weight, yield and growth has been reported in many plant species under stress conditions.

Abiotic stresses can also induce defense response such as PR gene activation without necrosis (Brederode *et al*., 1991; Green and Fluhr, 1995; Malamy *et al*., 1996). Some of these stresses have been found to act through SA (Malamy *et al*., 1996; Yalpani *et al*., 1994). SA has been shown to ameliorate abiotic stress in a number of plant species including, salt stress in cucumber seedlings (Xiaoping *et al*., 2002), *Brassica juncea* and wheat seedlings (Zhang *et al*., 1999), *Arabiopsis* seedlings (Borsani *et al*., 2001), *Phaseolus vulgaris* seedlings (Sally, 2004), diquat-induced oxidative stress in cucumber (Grezys *et al*., 2003), SA also ameliorated cadmium toxicity in soybean seedlings (Drazic and Mitailovic, 2005), heavy metal stress in rice (Mishra and Choudri, 1999), heat and cold stress in young grape plants (Wang and Shao-Hua, 2005), cold stress in maize, cucumber and rice (Szalai *et al*., 2000; Kang and Saltveit, 2002) and heat stress in *Agrostic stolonifera* (Larkindale and Huang, 2004).

Mechanism of Action

SA has been shown to inhibit tobacco catalase enzyme activity both *in vivo* and *in vitro* (Larkindale and Huang, 2004; Chen *et al*., 1993). Catalase scavenges hydrogen peroxide (H_2O_2), produced from photorespiration, fatty acid β-oxidation and superoxide anions (O_2^-) by Superoxide dismutase (SOD). Inhibition of catalase by SA increases the endogenous level of H_2O_2. The H_2O_2 and other Reactive Oxygen Species (ROS) derived from it, could then serve as second messengers to induce the expression of plant defense related genes (Conarth *et al*., 1995) (Fig. 4).

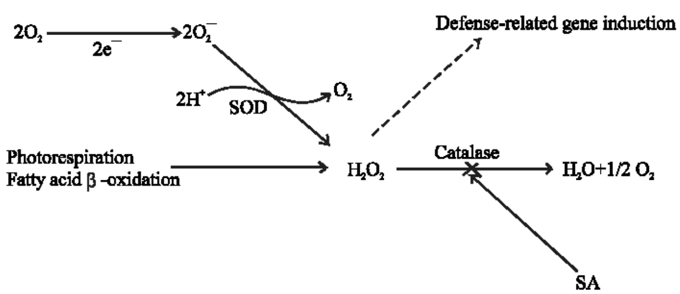

Fig. 4: Inhibition of catalase by SA. H_2O_2 is produced form photorespiration, β-oxidation of fatty acids and superoxideanions (O_2^-) by superoxide dismutase (SOD)

Salicylic Acid and Flowering

The role of SA as an endogenous signaling molecule was first suggested in relation to flowering. Cleland and coworkers found that honeydew from aphids feeding on Xanthium strumarium contained an activity that induced flowering in duckweed (*Lemna gibba*). The flower-inducing factor was then extracted from Xanthium phloem and identified as SA (Cleland, 1974; Cleland and Ajami, 1974). Exogenously applied SA has also been shown to induce flowering in both organogenic tobacco (*Nicotiana tabacum*) tissue culture (Lee and Skoog,1965) and in tobacco cell culture (Eberhard *et al*., 1989). The first concrete evidence implicating endogenous SA as a regulatory molecule emerged from studies of Voodoo lillies (*Sauromantum gutatum*) (Raskin *et al*., 1987, 1989). SA has also been shown to induce flowering in species of Lemnaccae like oncidium, an ornamental orchid species, Impatiens balsamina, *Arabiaopsis thaliana* and in *Pistia stratiotes* (Araccae) (Raskin, 1992).

Salicylic Acid and Thermogenesis

Thermogenicity literally means heat production in plants. it was first described by Lamarck in 1778 for the genus Arum (Lamarck, 1978). Thermogenicity is now known to occur in the male reproductive structures of cycades and in the flowers and inflorescence of some angiosperm species belonging to the family *Annonacaceae*, *Asaceae*, *Aristolochiaceae*, *Cyclanthaceae*, *Nymphacaceae* and *Palmae* (Meeuse and Raskin, 1988). The heat facilitates the volatilization of foul smelling amines and indoles that are attractive to insect pollinators (Lamarck, 1978). SA has been shown to be the producer of heat i.e. Calorigen in male flowers of Voodoo lily (Raskin *et al*., 1987). The spadix of the voodoo lily is thermogenic and exhibits an increase in temperature during flowering. Thermogenesis and the production of aromatic compounds associated with thermogenesis were found to be induced by treatment of spadix explants with SA (Klessig and Malamy, 1994).

Mechanism of Action

The mechanism by which SA induces flowering is still to be discovered. Thermogenicity involves activation of glycolytic and Krebs cycle enzymes, which provide substrates for metabolic explosion. During thermogenesis much of the electron flow in mitochondria is diverted from the cytochrome respiratory pathway (Meeuse, 1975). The energy of electron flow through the alternative respiratory pathway is not conserved as chemical energy, but released as heat. The alternative respiratory pathway utilizes an alternative oxidase as the terminal electron acceptor. Rhoads and Mcintosh (1992) found that SA induces expression of the alternative oxidase gene in Voodoo lilies. SA treatment also caused an increase in alternative respiratory pathway capacity and accumulation of alternative oxidase (Rhoads and Mcintosh, 1993).

Other Uses of Salicylic Acid

Exogenously supplied SA has been shown to affect a large variety of processes in plants, including, stomatal closure (Larque, 1979), seed germination, fruit yield and glycolysis (Cutt and Klessig, 1992).

Conclusions

Salicylic acid is perhaps the only compound on the surface of the earth to mediate so diverse functions as ranging from curing various human ailments to protect the plants from various biotic and abiotic stresses and affecting various physiological and biochemical processes of plants. The exact mechanism of action of SA in some plant processes is still insufficient and needs further investigation. In future, biochemical and physiological changes in plants by SA may be explored to use than as biochemical markers, which may further be transformed into genetic markers and be utilized in genetic engineering of plants for making them tolerant to various stresses.

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