A History of Commercial Plant Growth Regulators in Apple Production

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The term plant growth regulator (PGR) refers to natural and synthetic compounds applied to plants or plant organs to regulate growth or development. PGRs play an important role in commercial horticulture, particular in fruit production. This overview of the history of commercial PGRs consists of 1) a brief history of the discovery of five primary plant hormones or hormone groups (auxins, gibberellins, cytokinins, ethylene, and abscisic acid), 2) background on the commercial development of gibberellic acid (GA_3), 3) discussion of the development of PGRs for commercial fruit production during the later part of the 20th century, and 4) speculation on future commercial PGR opportunities.

DISCOVERY OF PLANT HORMONES

The discovery and understanding of plant hormones has been key to PGR development. Narratives of these discoveries have been presented elsewhere (Bukovac, 1987; Davies, 1995; Jacobs, 1979; Salisbury and Ross, 1992; Wilkins, 1984). Following is a brief history of the five primary hormones or hormone groups.

AUXINS. Auxins were the first group of hormones to be discovered. Some of the earliest work with plant growth regulators is traced back to Charles Darwin and his studies on phototropism of oat (*Avena*) coleoptile. The phototropic experiments conducted around 1880 demonstrated that the coleoptile was responsible for sensing light, and that the light response was transmitted basipetally from the illuminated coleoptile tip (Jacobs, 1979). In a series of papers from 1910–1913, Boysen-Jensen showed that the tip of the coleoptile was the source of the phototropic effect and that a diffusible substance produced in the tip could pass through a layer of agar to confer phototropism. Went used agar blocks in the development of the first bioassay, the *Avena* coleoptile bending test, and the eventual identification of indole acetic acid (IAA) as the endogenous auxin in plants (Bandurski and Nonhebel, 1984; Jacobs, 1979).

GIBBERELLINS. The discovery of gibberellic acid (GA_3) by Japanese workers illustrates the contribution of plant pathologists to PGR research. The fungus *Gibberella fujikuroi* causes Bakanae disease or foolish rice disease resulting in abnormally tall seedlings. During the 1930s, Japanese scientists isolated impure gibberellins from fungal culture filtrates (Phinney, 1983). However, the lack of communication among scientists during wartime caused their work to be largely overlooked. After the war, Imperial Chemicals Industries (ICI), now part of Syngenta, obtained cultures of the fungus. In 1955, ICI reported the isolation and characterization of GA_3 (Brian and Hemming, 1955). While there are currently over 130 gibberellins known to date, only GA_3 , GA_4 and GA_5 are used commercially.

CYTOKININS. The initial attempt to identify a cytokinin was performed in Went's lab by Bonner (1940). He discovered that a diffusate from the soak water of pea seeds increased the growth of excised leaf discs. In addition, Bonner determined that yeast extract had considerable activity in the leaf disc bioassay. Fractionation of the yeast extract demonstrated that adenine, hypoxanthine and xanthine increased growth of excised leaf disks. The isolation of hypoxanthine supported the argument for a purine-based hormone (cytokinin). However, the adenine activity in the leaf disc bioassay was difficult to reproduce (Jacobs, 1979). It remained for the lab of Skoog at the University of Wisconsin to develop callus culture techniques and to understand the need for an auxin/cytokinin balance in the development of plant organs. In Skoog's lab, Miller used fractionated yeast extract in the cell culture system. In addition to screening commercially available purines, including adenine, Miller tested degraded herring sperm DNA. The resulting cytokinesis was found to be due to kinetin produced during

DNA breakdown (Miller et al., 1955). Kinetin was significantly more active than adenine in the tobacco tissue culture bioassay. The use of the plant cell culture bioassay was a key to the eventual isolation of zeatin from corn by Letham (1963).

ETHYLENE. The growth regulating properties of ethylene were first recognized by the Russian scientist Nejebulov in 1901 (Beyer et al., 1984). His experiments showed that illuminating gas could cause leaf abscission and epinasty. The fruit physiologist Crocker developed the Alaskan pea bioassay that used the triple response of shortening and thickening of the hypocotyl, agravitropic growth, and maintained hypocotyl hook (Reid and Howell, 1995) to assess ethylene levels. He was the first to suggest that ethylene was an endogenous plant hormone. However, few scientist at the time agreed with Crocker since it was difficult to visualize that a gas could act as an endogenous regulating substance. It was not until the 1960s when gas chromatography was used to quantify endogenous ethylene that the significance of ethylene was recognized and acknowledged as an endogenous hormone.

ABSCISIC ACID. While researchers had long speculated that a hormone which affected abscission, dormancy, and stress reduction existed, it was not until the 1950s that work on the isolation and identification of this compound began. In 1953 Bennet-Clark and Kefford discovered an acid fraction of plant extracts that was a potent growth inhibitor. In 1955 Osborne reported on the diffusion of a senescence factor from older leaves that could speed the abscission of bean petioles. By 1963, Addicott's group studying cotton fruit abscission in California had identified and characterized abscisin II. At the same time, Wareing's group in Wales identified the dormin as a compound that promoted dormancy in woody plants. In 1968, these groups formally redesignated abscisin II and dormin as abscisic acid (Milborrow, 1984).

COMMERCIAL PRODUCTION OF GA_3

GA_3 was among the first compounds to be widely used as a PGR. Consequently, commercial production of cost-effective GA_3 has become an important part of the history of PGRs.

Impure gibberellins were isolated from fungal culture filtrates in Japan during the 1930s, but the first isolations of pure gibberellins were made at ICI in the United Kingdom during the mid-1950s. However, during the late 1950s, ICI decided not to enter the U.S. marketplace, but to market GA_3 products in the rest of the world. As a result ICI licensed GA_3 to a consortium, the Gibberellic Acid Registration Task Force. This task force, formed by Merck, Eli Lilly, Abbott Laboratories, Pfizer, and American Cyanamid, was to develop GA_3 products for the U.S. marketplace (Robert Cibulsky, personal communication). Eli Lilly was the first company to register a GA_3 product for use on seedless grapes in 1960. Abbott Laboratories and Merck registered GA_3 products shortly thereafter.

Many current uses for GA_3 were not known in 1960. Eli Lilly's first label included uses for their product on grapes only. The preharvest use of GA_3 on lemons was added to the Abbott label in 1963. The use of GA_3 on sour cherries (*Prunus cerasus*) was added to the product label by 1965.

GA_3 use was initially restricted by product cost. ICI had found that neither chemical synthesis nor extraction of GA_3 from plants was economical. In the late 1960s Abbott Laboratories commitment to improving the fermentation of GA_3 through a strain improvement program led to significant cost reductions over a 10-year period (Robert Cibulsky, personal communication). The resulting lower product cost was more acceptable to commercial growers and the commercial use of GA_3 increased.

DEVELOPMENT OF PGRs FOR COMMERCIAL APPLE PRODUCTION

Control of growth and development of fruit trees has been practiced for many centuries. However, the use of PGRs to alter fruit tree physiology is a relatively new concept. Today, PGRs are vital to the apple industry. Among the commercial PGRs listed in the Farm Chemicals Handbook 2002 (Table 1), at least seven are used for producing apples. The following illustrates the research behind the co-evolution of PGR use and commercial apple production.

FLOWER AND FRUIT REMOVAL

Orchardists for centuries have recognized the usefulness of flower and fruit removal early in the season of the on-year to help counteract biennial bearing. Thinning was done by hand before 1940. Two divergent approaches to flower/fruit removal have been followed since then. On approach involves damaging the blossom with caustic sprays (blossom thinners). The other involves fruit removal with the use of hormone sprays (postbloom thinners).

BLOSSOM THINNERS. Auchter and Roberts (1934) were among the first to use of caustic sprays at bloom to regulate cropping by preventing fruit set. Copper sulfate, tar distillates and other caustic compounds reduced fruit set but caused unacceptable levels of leaf and fruit injury. One compound, sodium-4,6-dinitro-ortho-cresylate (DNOC), sold as Elgetol, emerged as an effective and relatively safe compound for reducing crop load to counteract biennial bearing (Batjer and Thompson, 1948). DNOC

remained a blossom thinner of choice until its U.S. registration was withdrawn in 1990 by the Environmental Protection Agency because of a lack of support information necessary for re-registration. Replacement compounds including ammonium thiosulfate (ATS), endothalic acid (Endothall), pelargonic acid (Thinex), sulcarbarnide-1-aminomethanamide hydrogem tetraoxosulfate (Wilthin), and hydrogen cyanamide (Dormex) have been evaluated as DNOC replacements (Bound and Jones, 1997; Byers, 1997; Fallahi, 1997; Williams, 1993). While none of these compounds have come close to achieving the commercial success of Elgetol, ATS has been among the most consistent in its thinning response. Other promising products considered organic thinners including lime-sulfur, fish oils, and various surfactants and vegetable oils are being evaluated. However, evaluation of these products has not proceeded to the point where their future value can be estimated.

POSTBLOOM THINNERS. Soon after the discovery and characterization of the endogenous hormone indoleacetic acid (IAA), several synthetic auxins including naphthaleneacetic acid (NAA) and naphthaleneacetamide (NAD) were found to cause fruit abscission (Burkholder and McCown, 1941). Response to these thinners is influenced by cultivar, fruit size at time of application, and temperature following application (Williams and Edgerton, 1981). NAA remains an important thinning chemical especially where more aggressive thinning is appropriate.

The insecticide carbaryl is a mild thinner on apples (Batjer and Westwood, 1960). Carbaryl is rate-insensitive at concentrations over 750 mg·L⁻¹ (Southwick et al., 1964), thins over a wide range of fruit sizes (Knight and Spencer, 1987), breaks up fruit clusters (Looney and Knight, 1985) and rarely overthins. However, carbaryl has some limita-

Table 1. Commercial plant growth regulators.²

Common name(s)	CAS chemical name
2,4-D	(2,4-Dichlorophenoxy)acetic acid
2,4-DP	2-(2,4-Dichlorophenoxy)propanoic acid
4-CPA	4-Chlorophenoxyacetic acid
Aviglycine; AVG	(2S,3E)-2-Amino-4-(2-aminoethoxy)-3-butenic acid
Ancymidol	α -Cyclopropyl- α -(4-methoxyphenyl)-5-pyrimidinemethanol
Benzyladenine; 6-BA	N ⁶ -(Phenylmethyl)-1H-purin-6-amine
BNOA	
Butralin	2-Naphthalenyloxyacetic acid
Carvone	4-(1,1-Dimethylethyl)-N-(1-methylpropyl)-2,6-dinitrobenzenamine
Chlormequat chloride	2-Methyl-5-(1-methylethenyl)-2-cyclohexene-1-one
Chlorpropham; CIPC	2-Chloro-N,N,N-trimethylethanaminium chloride
Daminozide	(3-Chlorophenyl)carbamic acid 1-methylethyl ester
Decanol	Butanedioic acid mono(2,2-dimethylhydrazide)
Diphenylamine; DPA	1-Decanol
Ethephon	N-Phenylbenzenamine
	(2-Chloroethyl)phosphonic acid
Ethoxyquin	6-Ethoxy-1,2-dihydro-2,2,4-trimethylquinoline
Ethylchlorate	Ethyl 5-chloro-3(1H)-indazolylacetate
Flumetralin	2-Chloro-N-[2,6-dinitro-4-(trifluoromethyl)phenyl]-N-ethyl-6-fluorobenzenemethanamine
Flurprimidol	α -(1-Methylethyl)- α -[4-(trifluoromethoxy)phenyl]-5-pyrimidinemethanol
Forchlorfenuron; CPPU	1-(2-Chloro-4-pyridyl)-3-phenylurea
Gibberellin A3; Gibberellic acid; GA ₃	(1 α ,2 β ,4 α ,4 β ,10 β)-2,4a,7-Trihydroxy-1-methyl-8-methylenegibb-3-ene-1,10-dicarboxylic acid 1,4a-lactone
Gibberellin A4/7; GA ₄ /GA ₇	GA ₄ ; (1 α ,2 β ,4 α ,4 β ,10 β)-2,4a-Dihydroxy-1-methyl-8-methylenegibb-1,10-dicarboxylic acid 1,4a-lactone GA ₇ ; (1 α ,2 β ,4 α ,4 β ,10 β)-2,4a,7-Trihydroxy-1-methyl-8-methylenegibb-1,10-dicarboxylic acid 1,4a-lactone
Hydrogen cyanamide	Cyanamide
Indolebutyric acid; IBA	1H-Indole-3-yl butyric acid
Kinetin	N-(2-Furanylmethyl)-1H-purin-6-amine
Maleic hydrazide	1,2-Dihydro-3,6-pyridazinedione
Mefluidide	N-[2,4-Dimethyl-5-[[[(trifluoromethyl) sulfonyl] amino]phenyl]acetamide
Mepiquat chloride	1,1-Dimethylpiperidinium chloride
Naphthaleneacetic acid; NAA	1-Naphthaleneacetic acid
Naphthaleneacetic amide; NAD	1-Naphthaleneacetamide
Paclobutrazol	(α R, β R)-rel- β -[(4-Chlorophenyl)methyl]- α -(1,1-dimethylethyl)-1H-1,2,4-triazole-1-ethanol
Phthalamilic acid	N-Phenylphthalamic acid
Prohexadione calcium	3,5-Dioxo-4-(1-oxopropyl) cyclohexanecarboxylic acid
Quinmerac	7-Chloro-3-methyl-8-quinolinecarboxylic acid
Thidiazuron; TDZ	N-Phenyl-N'-1,2,3-thiadiazol-5-ylurea
Thiourea	Thiourea
Trinexapac-ethyl	4-(Cyclopropylhydroxymethylene)-3,5-dioxocyclohexanecarboxylic acid ethyl ester
Uniconazole-P	(E)- β -[(4-Chlorophenyl)methylene]- α -(1,1-dimethylethyl)-1H-1,2,4-triazole-1-ethanol

²Plant growth regulators with defined chemistries as listed in Farm Chemicals Handbook 2002 (Meister Publishing, 2002).

³Entry dates for compounds released before 1996 as listed in Global Herbicide Directory, 1998; NL = not listed. Entry dates for AVG, 6-BA, GA₃, and GA₄/GA₇, Ricardo Menendez, personal communication.

tions. Since it is toxic to bees, applications must be delayed until bees are removed from the orchard. Further, carbaryl may be harmful to mite predators (Hislop and Prokopy, 1981) thus increasing the risk of mite infestations. Nevertheless, carbaryl is the most widely used chemical thinner in the U.S. (Greene, 2002a) although it is coming under increased regulatory scrutiny in Europe and the U.S. that may result in curtailed use or withdrawal of registration. Vydate, another carbamate registered for use on apples, has thinning activity similar to that reported for carbaryl (Byers et al., 1982).

Chemical thinning generally results in larger fruit size at harvest, due primarily to the reduction in competition among developing fruit. The cytokinin benzyladenine (6-BA) is the active thinning component in the most recently registered thinner. Like other thinners, 6-BA increases fruit size by a reduction in competition, but unlike other thinners, it also increases fruit size by stimulating cell division (Wisner et al., 1995). 6-BA is generally considered a mild thinner when used by itself (Greene, 2002a).

During the first decades of commercial chemical thinning, emphasis was placed on conducting numerous trials to evaluate chemicals, concentrations, cultivars and local adaptations. The process was considered more art than science (Martin, 1979). Significant progress has been made in the past 25 years in gaining a better understanding of factors that influence thinner response and how to make chemical thinning more predictable (Forshey, 1986; Williams, 1979). Weather conditions following application play a dominant role in determining a thinner's ultimate effectiveness (Byers et al., 1991; Greene, 2002a; Schwallier, 1996). Critical to better understanding of thinner response are investigations on the mechanism of thinner action (Stopar, et al., 1997; Yuan and Greene, 2000).

DEVELOPMENT AND MAINTENANCE OF TREE STRUCTURE

The goal of orchardists is to develop a tree that efficiently intercepts a large portion of available light and yet has the structure that encourages the development of productive and fruitful wood. Twenty five years ago this goal was accomplished by planting trees on semi-dwarf rootstock at moderate densities, then developing a strong framework to support fruit. Plant bioregulators which contained 6-BA and GA₄/GA₇ were useful in developing the framework of these trees by stimulating lateral branching on young trees (Forshey, 1982; Miller and Eldridge, 1986). The gibberellins in these sprays inhibited flower bud formation for the following year, but were not considered a problem since tree structure was in the developmental stages and full production was not expected for several years. Recent economic analysis has shown that the most profitable orchards are those that fill their allotted space early. To achieve this, orchards are now planted at much higher densities on dwarfing rootstocks. Branching agents containing 6-BA + GA₄/GA₇ such as Promalin (Valent Biosciences Corp.) are now applied in the nursery at earlier tree development to stimulate branching (Cody et al., 1985). As a consequence, newly planted feathered trees already possess the scaffold structure that allows them to have significant production within 2 years after planting.

VEGETATIVE GROWTH CONTROL

Vegetative growth and cropping are delicately balanced. A balance

Example brand	Company	Activity	Example use(s)	Entry date ^b
Citrus Fix	Amvac Chemical Corp.	Auxin	Prevent citrus abscission	1942
Dicopur DP	NuFarm	Auxin	Improve grape sizing	1945
Fruitone	Amvac Chemical Corp.	Auxin	Improve grape sizing	1945
ReTain	Valent Biosciences Corp.	Ethylene synthesis inhibitor	Delay pome fruit ripening and improve quality	1997
A-Rest	SePRO Corp.	Gibberellin synthesis inhibitor	Inhibit ornamental growth	1971
Accel	Valent Biosciences Corp.	Cytokinin	Promote apple fruit size	1979
Blossom set	Cyclo International SA	Auxin	Improve blossom set	NL
Tamex	CFPI-Nufarm	Growth inhibitor	Inhibit tobacco sucker growth	1971
Talent	Luxan BV	Growth inhibitor	Inhibit potato sprouting	NL
Cycocel Extra	BASF Corp.	Gibberellin synthesis inhibitor	Reduce cereal lodging	1960
Endogerm CP	Chimac-Agriphar SA	Mitosis inhibitor	Inhibit potato sprouting	1951
B-Nine	Uniroyal Chemical	Gibberellin synthesis inhibitor	Improve fruit development	1962
Sucker Agent 504	Drexel Chemical Co.	Undetermined	Inhibit tobacco sucker growth	NL
No-Scald DPA 283	Cerexagri Inc.	Antioxidant	Inhibit stored apple scald	NL
Ethrel	Bayer	Ethylene releaser	Enhance fruit color, promote sweet and sour cherry fruit abscission, flower induction in pineapple	1965
Decoquin 305	Cerexagri, Inc.	Antioxidant	Inhibit apple scald	NL
Figaron	Fujisawa Pharmaceutical	Auxin	Thinning and ripening acceleration of citrus fruit	1976
Prime+	Syngenta	Growth inhibitor	Inhibit tobacco sucker growth	1977
Cutless	Dow Agrosciences LLC	Gibberellin synthesis inhibitor	Inhibit turf growth	1981
NL	SKW	Cytokinin	Improve grape and kiwi fruit size	1983
ProGibb	Valent Biosciences Corp.	Gibberellin	Improve size of grapes, improve quality of cherry and citrus, alter flowering in sour cherry	1962
Provide	Valent Biosciences Corp.	Gibberellin	Improve apple fruit finish	1979
Dormex	SKW Trostberg AG	Undetermined	Synchronize grape bud break	1982
Seradix	Bayer	Auxin	Promote rooting	1935
X-Cyte	Stoller Enterprises, Inc.	Cytokinin	Biostimulant	NL
Super Sprout Stop	Uniroyal Chemical	Growth inhibitor	Inhibit potato sprouting	1949
Embark	Whitaker Distribution	Growth inhibitor	Inhibit turfgrass growth	1974
Pix	BASF Corp.	Gibberellin synthesis inhibitor	Inhibit ornamental growth	1972
Fruitone N	Amvac Chemical	Auxin	Fruit thinning in apples and citrus	1939
Amid-Thin W	Amvac Chemical	Auxin	Fruit thinning in apples	NL
Bonzi	Uniroyal Chemical	Gibberellin synthesis inhibitor	Inhibit ornamental growth	1982
Nevrol	EMV Ltd.	Auxin transport inhibitor	Fruit thinning	1982
Apogee	BASF Corp.	Gibberellin synthesis inhibitor	Inhibit apple vegetative growth	1997
Bonus	BASF Corp.	Auxin	Improve rooting and fruit set	1985
Dropp	Bayer	Cytokinin	Defoliation of cotton	1976
Command	Ladda Co., Ltd.	Undetermined	Break dormancy	NL
Primo MAXX	Syngenta Professional Products	Gibberellin synthesis inhibitor	Inhibit turf growth	1988
Sumagic	Sumitomo Chemical Co., Ltd.	Gibberellin synthesis inhibitor	Inhibit ornamental growth	1984

within a tree that favors vegetative growth can reduce flowering, fruit set, fruit quality, pest control, and grower profit. Excessive vegetative growth can result from a weather event such as frost or inappropriate management decisions in thinning, fertilization, or pruning.

Trees propagated on vigorous and semi-dwarf rootstocks are generally slow to come into production. Growth retardation on these rapidly growing trees generally results in increased flower bud formation and fruit set. The growth retardants daminozide (Alar) and ethephon (Ethrel) came into regular use in the early 1970s at a time when a number of apple trees were being planted on these more vigorous rootstocks. Used individually, both compounds inhibit vegetative growth and enhance flower bud formation. However, combination sprays were more effective and frequently the treatment of choice on young nonbearing trees (Greene, 1981). Daminozide did not cause fruit abscission and could be used safely to control growth on bearing trees. The registration for the use of daminozide on apples was withdrawn in 1989 due to concerns that it may be a carcinogen and that it caused an unacceptable level of risk for the development of cancer.

In addition to being an effective growth retardant, ethephon is also an effective thinner. Therefore, its use to control vegetative growth generally is restricted to application on young trees, trees that are biennial, or trees that have lost a crop due to frost. Some have expressed the concern that the use of ethephon on bearing trees may result in excessive flower bud formation, making thinning difficult, and thus initiating a biennial bearing cycle.

Pacloutrazol is a gibberellin biosynthesis inhibitor that was first reported by Quinlan (1980) to control growth on apple trees. Effective growth retardation may be achieved by application as a foliar spray, a soil drench around the trunk of a tree, by trunk injection, or in paint applied to the trunk (Miller, 1989). Spray application emerged as the favored method of application, and multiple sprays starting about 3 weeks after bloom were more effective than one application (Quinlan and Richardson, 1986). Since it is slowly metabolized within the tree, some growth retarding effects can persist within the tree for several years. Pacloutrazol is not registered for use on apples in the U.S., primarily due to concerns over ground water contamination, but is sold commercially in other countries.

Prohexadione-Ca (Apogee in the U.S., Regalis in Europe) is a growth retardant recently registered by BASF that acts by inhibiting gibberellin biosynthesis (Evans, et al., 1999). Since prohexadione-Ca degrades rapidly, it must be applied several times as soon as sufficient leaf tissue emerges, which is usually near petal fall. Prohexadione-Ca can increase fruit set, even when applied at moderate rates suggested on the label, and thus requires a more aggressive thinning program to achieve an appropriate level of fruit set (Greene, 1999). Most of its effects are secondary and generally attributed to increased light penetration due to a reduction in terminal growth. Prohexadione-Ca may control fire blight on shoots by inducing resistance in the tree (Yoder et al., 1999).

FLOWERING AND FRUIT SET

The present trend in apple production is to plant trees on precocious dwarfing rootstocks. For this reason there is little need to encourage additional flower buds on nonbearing trees. However, there is a need to enhance flowering on bearing trees, either to partially overcome biennial bearing or to increase flowering in marginal situations. Harley et al. (1958) reported that NAA increased flower bud formation in the absence of a thinning response, but little research has been done to fine tune this observation. Recently, production guides have recommended NAA to enhance flowering on bearing trees.

Ethephon promotes flowering but is also a strong thinner. However, multiple low doses starting at the end of June drop may be useful. Byers (1993) has shown that application of 100 to 200 mg·L⁻¹ of ethephon in 12 weekly or 6 biweekly sprays will enhance flower bud formation without thinning although it advanced fruit ripening.

The increased use of precocious rootstocks in apple orchards has led to excessive fruit set. This increases limb breakage, diminishes tree growth, and does not allow trees to fill their allotted space. Sprays of 250 to 500 mg·L⁻¹ GA₃ or GA₄/GA₇ can substantially reduce return bloom on young trees, thus improving tree growth and structure (Unrath and Whitworth, 1991). However, a similar use of gibberellins to regulate biennial bearing

has not been as reliable on bearing trees (Greene, 2000).

Gibberellins can increase fruit set, but their general use for this purpose has not become widespread because of unpredictable response, reduced fruit size, and inhibition of flower bud formation. Prohexadione-Ca increases fruit set especially in cooler growing regions (Greene, 1999). Often increased fruit set on bearing trees is considered undesirable since small fruit size and reduced fruit size are the usual consequences. However, in situations where bloom is light and pollinating conditions marginal sprays of prohexadione-Ca may well be beneficial to increasing fruit set and help control vegetative growth on lightly cropping trees. Aminoethoxyvinylglycine (AVG) can increase fruit set when applied as a petal fall spray (Greene 1980; Williams, 1980).

PREHARVEST DROP

Preharvest drop is a serious problem. Some cultivars such as 'McIntosh' are particularly prone to preharvest drop. In areas where one or two cultivars dominate, the problem is further complicated since growers are faced with the challenge of harvesting a large portion of their crop before fruit condition declines and fruit are lost due to drop.

Auxins can inhibit preharvest drop. Although many auxins were tested and some were used, the only auxin to survive regulatory scrutiny and the reregistration process was NAA. NAA does not enjoy widespread use today for several reasons. First, two applications may be necessary since the effect lasts only 7 to 10 days. If two applications are used, an additional 7 days of drop control can be expected. Second, ripening is often advanced and reduces storage life. Marini et al., (1993) reported that repeat application well in advance of the start of drop may be an effective way to control preharvest drop on 'Delicious' without subjecting the trees to unwanted side effects. Unrath (1996) suggested 4 weekly applications of 5 mg·L⁻¹ NAA starting 4 weeks before anticipated harvest.

Daminozide was the preharvest drop compound of choice for most cultivars for over 20 years starting in the late 1960s. Not only did it retard drop, but it also increased flesh firmness and red color (Edgerton and Hoffman, 1965). Withdrawal of registration of daminozide in 1989 left growers with NAA as the only preharvest drop control option.

Bangerth (1978) first reported that multiple applications of aminoethoxyvinylglycine (AVG), an ethylene biosynthesis inhibitor, retarded preharvest drop of apples. ReTain, an AVG product developed and formulated by Abbott Laboratories (now Valent BioSciences Corp.) was granted full registration by the U.S. Environmental Protection Agency in 1997. AVG has become the dominant PGR used to retard preharvest drop on apples in the U.S.

IMPROVING FRUIT APPEARANCE AND SHAPE

'Delicious' dominates the apple in the market today. The public prefers blocky fruit with prominent calyx lobes. Sprays containing equal amounts of 6-BA and GA₄/GA₇ at bloom have been used since the 1970s to improve fruit shape. The cytokinin (N-(2-chloro-4-pyridyl)-N-phenylurea (CPPU) applied at bloom may be even more effective at elongating 'Delicious' (Curry and Greene, 1993), but it has not been registered on apples.

Regions where the weather is typically rainy, moist, and humid during the post bloom period have fruit that appear russeted. If severe, the grade of fruit can be reduced. Two to four postbloom applications of products containing GA₄/GA₇ will reduce russetting.

INFLUENCING FRUIT MATURITY AND QUALITY

The goal of orchardists is to harvest fruit at optimum maturity for best eating quality or at a stage of maturity that will assure near-optimum eating quality out of storage. Because a large number of fruit must be harvested in a short period of time, strategies to advance or delay ripening are appropriate.

Many studies in the 1970s developed protocols to advance ripening and increase red color of apples using ethephon. In general 62.5 to 125 mL/100 L was applied 1 to 3 weeks before normal harvest. These sprays included a drop control compound. Fruit were then harvested 7 to 10 days after application and were intended for short term storage. This general approach to advancing fruit ripening of apples for early sale is still used.

Daminozide was used to delay apple ripening (Edgerton and Hoffman, 1965). This not only extended the harvest season but it delayed the loss of fruit firmness and some instances reduced the incidence of physiological disorders such as watercore (Lord et al., 1967). AVG has now replaced daminozide and is the only product on the market that can delay ripening on the tree. AVG can reduce watercore, one of the major causes of internal breakdown in storage (Greene, 2002b). Fruit receiving AVG are generally firmer at harvest, but the extent of this firmness increase appears to be quite variable.

Recently, the ethylene action blocker, 1-methylcyclopropene (1-MCP) was introduced as SmartFresh by AgroFresh for postharvest application to maintain apple quality through long-term storage (Blakenship and Unrath, 1998).

FUTURE COMMERCIAL PGR OPPORTUNITIES

Previous authors have speculated on the future of commercial PGRs (Carlson and Crovetto, 1990; Cibulsky and Crovetto, 1981; Crovetto and Shafer, 1988; Rademacher and Bucci 2002; Schott and Walter, 1991; Thomas, 1982). In general, to bring new commercial PGRs to market successfully, the products consistently must fill an economically important need of the customer and they must be sufficiently inexpensive to register and produce. Moreover, the targeted agricultural industries must be viable, the partnerships between companies and academia must be strong, and the companies must be willing to take the risk to develop a concept into a product.

CURRENT CHALLENGES FOR NEW PGR DEVELOPMENT

Market forces are delaying the development of new PGRs. The development of agricultural chemicals is closely tied to the health of the agricultural industry. As agricultural production has become more global, the margins of growers in mature markets have eroded. Also affecting interest in the developing new active ingredients include the increased cost of discovering, developing, and registering new compounds, increased generic competition, rise of transgenic crops, and domination of glyphosate in the herbicide market. These challenges have resulted in a reduced willingness of some companies to invest in the development of new PGRs.

OPPORTUNITIES FOR NEAR TERM GROWTH IN PGRs

In the near term, currently known PGRs make up the greatest number of product opportunities in the marketplace. First, among the currently commercialized products, continued label expansion of newer PGRs, such as AVG, will broaden their use on new crops. Second, PGR development opportunities exist in known, but not commercialized PGRs such as S-ABA, jasmonates, and brassinosteroids. Reduced production costs may make these PGRs commercially viable. Third, new markets such as organic farming or high quality fruit and vegetables may provide significant opportunities for new PGR uses. Fourth, plant systemic acquired resistance (SAR) inducers such as Actigard may become effective tools disease control programs.

OPPORTUNITIES FOR LONG-TERM GROWTH IN PGRs

In the longer term, new uses for PGRs will be discovered in at least three ways: 1) systematic screening, 2) dissection of biological phenomena, and 3) chance discovery. While all of these methods have existed in the past, there have been changes in the way in which these are performed. New methods, such as the use of genomics to identify targets and bioinformatics to identify patterns in high throughput screening data, provide new tools for discovery.

Systematic screening will continue to be an important means of identifying new agricultural chemicals. Such screening of large numbers of synthesized chemicals for use against weeds, pathogens, and other pest targets has led to many new products. However, these screenings require large inputs of labor, time, and space. To reduce the inputs, acceleration of the primary screens is necessary for high-throughput screening. One technique for accelerating the assay is to use molecular targets, developed through genomics, as opposed to phenotypic targets.

Molecular targets allow for screening in cell culture in a single 96-well plate that, in the past, would have required the production of hundreds of greenhouse-grown plants. Moreover, the new primary screens might only require a few milligrams of compound, as opposed to the hundreds of milligrams that a traditional screen might have used.

The dissection of biological phenomena has continued to reveal roles for PGRs. *Arabidopsis* and molecular tools have allowed for new approaches to look at interesting problems. For example, in the previous decade, researchers demonstrated a development role for both brassinosteroids and cytokinins in de-etiolation of *Arabidopsis* (Chory et al., 1994; Fujioka et al., 1997). This work may lead to a greater understanding of the value of brassinosteroids in commercial agriculture. Other researchers will undoubtedly also demonstrate roles for endogenous PGRs as more complex phenomena are examined molecularly.

Chance discovery will also continue to play a role in PGR development. There continue to be opportunities for careful observations to make an impact on PGR development. For example, ethephon may have a significant impact on the activity of photosystem I inhibiting herbicides (Silverman and Petracek, personal communication). While the idea of modulating herbicide activity with PGRs is not new (Sterrett et al., 1983), this particular finding confirms that there may be more opportunities for PGR discovery than we might expect.

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