

An Elective Course on Writing and Publishing a Review Article

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In an effort to provide an opportunity for talented and motivated pharmacy students to learn about publishing a scientific review article, Temple University School of Pharmacy (TUSP) initiated an elective course in 1997 titled "Writing and Publishing a Review Article". It soon became apparent that almost all of the students who enrolled in the elective had the scientific acumen, literature-search skills, and the motivation to go beyond just learning about the process and to actually try to publish a paper. As a result, the course now has as a stated goal the writing and submission of a manuscript to a peer-reviewed journal. Since its inception in 1997, a total of 39 students have taken the course. To date 38 students, working in teams, have had 11 papers published in peer-reviewed journals.

Keywords: Elective courses; Journals; Publication; Review article; Writing

INTRODUCTION

The modern pharmacy student is being prepared for a future that will demand critical reading of the medical literature and many courses directly or indirectly train students to acquire the requisite skills. However, many students will acquire expertise during their subsequent careers that could contribute to the literature and many will be in residency, fellowship, or academic positions that reward or require publication. Yet, traditionally, few opportunities are available for students to learn about the scientific publishing process. Even fewer opportunities are available for students to learn first-hand how to publish or to participate in a scientific publication. In an effort to address this issue and to offer an opportunity for talented

and motivated students to consider having a published paper added to their curriculum vitae, TUSP initiated an elective course with the original intent of teaching the processes involved in getting a scientific review paper published. It was not originally assumed that the students would have the background or would be willing to devote the time and effort necessary to complete the process and actually submit a manuscript to a journal. However, possibly because of the prerequisite requirements (including demonstrably acceptable writing ability), the students' innate interest in publishing a paper, or the desire to add something to their résumés that would "stand out" compared to others, the students were prepared to attempt to publish a paper. Based on the early success, the course has been modified so that it now has as a stated goal the writing and submission of a manuscript to a peer-reviewed journal. This article outlines our experience with this elective course.

MATERIALS AND METHODS

Students and Class Size

The course is restricted to PharmD students (TUSP went to an all-PharmD programme starting in the Fall [Autumn] semester of 1998). The class size is limited to between 3 and 16 students. A class size of fewer than 3 students has been found to be too small for adequate teamwork or access to literature resources. A class size of more than 16 students has been found to be unwieldy.

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TABLE I Syllabus

Week	Activity
1	General introduction to the course: expectations, requirements, grading, etc. Discussion of reasons for publishing; Types of articles and types of journals; Overview of steps involved in publishing; Selection of groups; Request for topic ideas
2	Discussion of suggested topics: pros and cons of each (given the course constraints) Narrow selections to 2 for each group; Begin to formulate an outline for each; Begin literature search of relevant review articles; Begin to request reprints if necessary
3	Decide on topic for each group; propose possible titles Formulate outline (including approximate size of each section); Distribute workload Expand literature search to primary sources; Request reprints; Read reviews
4	Finalise outline and title Finalise each student's responsibilities
5	Continue literature searches; Begin writing
6	Continue writing (summarize individual reference articles)
7	Continue writing (summarize individual articles)
8	Continue writing (Abstract, synthesize material)
9	Review 1st draft (overheads or handouts)
10	Revise ms; continue writing
11	Review 2nd draft (overheads or handouts)
12	Make final changes
13	Review final draft (overheads or handouts)
14	Compose letter for journal submission; Make photocopies; Mail manuscript to journal
-	Review course experience
-	Follow-up on the status of the submitted manuscript (informal meetings, e-mails, etc.)

Prerequisites

The prerequisites primarily require: (1) that the students have sufficient science background to be a co-author of a scientific review article, and (2) they are able to write in a clear and grammatically correct style. The necessary science knowledge-base requirement is usually met by the time the student has the opportunity to take the elective course (3rd professional year at TUSP, which is 5th year of college-level coursework). The writing-skills requirement is subject to screening by the course instructor (RBR). The students are not required to have research data. The purpose of the course is to write a review article, not to write-up research work.

Syllabus

The syllabus (shown in Table I) is handed out at the beginning of the first class. It is important that the students realize that in order for them to be in a position to submit a manuscript by the end of the course, they need to start working quickly and efficiently.

Selection of Group Size

The usual optimal size for each group is 3 or 4 students. Fewer than this number places an extra burden on each group member, but it is sometimes acceptable and, given the right circumstances, has worked. More than this number becomes somewhat unwieldy and allows the opportunity for some students to become less productive. When the total

class size is large, it can be divided into smaller groups of 3 or 4 students each.

Selection of Topics

The final selection of topics is based on several criteria: (1) scientific rigor—the review must contain a component of basic science and clinical results must be accompanied by statistical analysis, (2) therapeutic interest—the review must relate to present or proposed pharmacotherapy, (3) likelihood of publication—the review must have a reasonable chance of acceptance by a peer-reviewed journal, and (4) mutual interest—the students must be motivated to work on the topic and the instructor must be qualified to advise the group.

Class Meetings

The first half-hour of each class is devoted to lecture material about the publication process (for example, choosing a journal, author instructions, reference styles, submission letter, peer-review process, revising a manuscript, reprints, etc.). The remainder of the time is devoted to the individual group topics. The students are told that this is *their* manuscript and that the instructor's role is like an art instructor's—to direct and channel the students' work, not create it. Most of the time is spent refining the goals, reviewing progress, editing drafts, and planning or scheduling the out-of-class assignments, such as the literature searches and writing.

Manuscript Submission

Each team (comprising students plus instructor) works together on all aspects of manuscript writing and submission. Topic selection, manuscript outline, allocation of assignments, information gathering, writing, and other aspects of the preparation are discussed at the weekly class meeting. Decision is by group consensus with guidance from the instructor. The instructor collates the written material, integrates the figures or tables, double-checks the references, and edits draft versions so that the finished product reads as much as possible as a single-authored work. As few changes as possible are made in content or style. This process is shared with the students as part of the learning experience and includes explanations of any changes. The final draft is reviewed by the entire team before it is submitted to the target journal. The actual journal review process spans weeks or months, long beyond the end of the course. The instructor keeps the students abreast of developments through regular contact, often by e-mail. Once available, reprints are mailed to the students for their use.

Authorship

As each manuscript results from approximately equal or equivalent contribution by each team member, including the instructor, all names appear as co-authors on the manuscript. This has been the case for all manuscripts to date, but is not guaranteed. The instructor's name is listed last, with the order of the student names being a joint decision by the team and is part of the learning process. Any resulting publications are not used as part of any performance indicator for the course instructor.

Grading and Evaluation

The students are informed during the first class meeting that the course grade and authorship on the paper is modeled on "real-world" criteria, that is (a) an objective measure assessing completion of assigned tasks (75% of grade) and, (b) a subjective measure assessing the level of contribution to the group's success (25% of grade). The educational success of the elective is assessed by the demonstrated opportunity for students to learn how to publish in peer-reviewed journals. There are no criteria regarding the number of publications.

RESULTS AND DISCUSSION

In all respects the experience with this elective at TUSP has been quite positive. The submission of the manuscript to a peer-reviewed journal has been

found to contribute to the educational process in the following ways. First, it provides an ambitious professional goal as incentive and establishes an unavoidable deadline. Second, it provides the opportunity for external critique and feedback. Third, acceptance brings tangible rewards including a feeling of accomplishment, a permanent record of accomplishment (in the form of a reprint), and a significant addition to the students' *curriculum vitae* or résumé.

To date a total of 39 students have taken the elective. The number of students who have enrolled in the elective has varied from year to year, from as many as 19 students to as few as 3. (Only 1 student took the elective in the Fall-2000 semester, but this was the year of transition to the "all PharmD" programme and there were only about 50 eligible students). All but 1 of the students have been successful in publishing a paper in a peer-reviewed journal, collaborating on a total of 11 papers (summarized in Table II) (Bennett *et al.*, 1998; Dixon *et al.*, 1999; Baby *et al.*, 1999; Betz *et al.*, 2000; Zebraski *et al.*, 2000; Carfagno *et al.*, 2000; Logani *et al.*, 2000; Hunsinger *et al.*, 2000; Schulingkamp *et al.*, 2000; Schock Citver *et al.*, 2002; Maiorini *et al.*, 2002). In order to give a sense of the contents and the level of these papers, their Abstracts are given in the "Appendix" section.

The topics jointly selected by the students and instructor have been quite varied. One theme, with the shared title "Indirect modulation of dopamine D₂ receptors as potential pharmacotherapy for schizophrenia" has resulted in a series of papers (2 published and another in progress) (Dixon *et al.*, 1999; Carfagno *et al.*, 2000). This particular theme represented a mutual interest at a time of newly emerging clinical and preclinical information. One student brought to the class's attention a meeting on the topic at a local State Mental Institution and the group and instructor registered for and attended the meeting. The information was incorporated into their manuscript.

Another popular theme was herbal products. A literature search for the first paper, on St. John's wort (Bennett *et al.*, 1998), uncovered a particularly necessary reference source that was available only in German. One of the students had a relative translate the article into English. Additionally, as part of this manuscript, it was recognized that little preclinical analysis was available, so the instructor had the active ingredient (hypericin) screened in receptor binding and other assays. The results were published separately and included in the paper.

The topic of novel pharmacotherapy for autism originated from a student following up a news-media account of "miracle cures" of autistic children given secretin. Despite the subsequently disappointing efficacy of secretin treatment in controlled trials,

TABLE II Writing and publishing a review article

Term	Title	Students	Status
Fall '97	Neuropharmacology of St. John's wort (<i>Hypericum</i>)	5	Ann. Pharmacother. 32: 1201-8, 1998
Spring '98	Indirect modulation of dopamine D ₂ receptors as potential pharmacotherapy for Schizophrenia: I. Adenosine agonists	3	Ann. Pharmacother. 33: 480-8, 1999
Fall '98	Actions of <i>Ginkgo biloba</i> related to possible neurologic utility	4	Life Sci. 67: 1389-1396, 2000
	Indirect modulation of dopamine D ₂ receptors as potential pharmacotherapy for schizophrenia: II. Glutamate (ant)agonists	4	Annals Pharmacother 34: 788-797, 2000
	Substance P antagonists: the next breakthrough in treating depression?	3	J. Clin. Pharm. Ther. 24: 461-469, 1999
	Lung opioid receptors: pharmacology and possible target for nebulised morphine in dyspnoea	2	Life Sci. 66: 2221-2231, 2000
	Does a common biochemical mechanism underlie addictions?	3	J. Clin. Pharm. Ther. 25: 11-20, 2000
	Is There a Basis for Novel Pharmacotherapy of Autism?	3	Life Sci. 67: 1667-1682, 2000
Fall '99	Brain Insulin Receptors and Clinical Implications	3	Neurosci. Biobehav. Rev. 24: 855-872, 2000
Fall '00	Indirect modulation of dopamine D ₂ receptors as potential pharmacotherapy for schizophrenia: III. Retinoids	1	<i>cont'd in Fall '01</i>
Fall '01	Indirect modulation of dopamine D ₂ receptors as potential pharmacotherapy for schizophrenia: III. Retinoids	2	J. Clin. Pharm. Ther. 27: 161-168, 2002
	Potential novel targets for Alzheimer pharmacotherapy: I. Secretases	5	J. Clin. Pharm. Ther. 27: 169-184, 2002

the team became interested in autism and contacted national leaders for input regarding the manuscript (Hunsinger *et al.*, 2000). Some continue to receive autism newsletters from national organizations.

The topic of brain insulin receptors was prompted by reading a remote reference to such and the general lack of awareness on the part of many of the existence of such receptors. The amount of literature searching required and background material needed was substantial. However, despite the relatively small team size of 3 students, the review turned out to be one of the longest, with 17 printed pages (Schulingkamp *et al.*, 2000).

One suggested topic seemed, at first, to be counter-intuitive, namely the use of nebulized morphine for treating dyspnoea. A literature search uncovered a surprising body of evidence related to the topic, and an even more surprising paucity of preclinical studies of respiratory tract opioid receptors. Although pulmonary opioid receptors were included in some of the earliest screens of opioid receptor distribution, the area has been woefully neglected since. Thus one major result of this paper (Zebraski *et al.*, 2000) was the identification of a critically under-studied area of research.

In terms of student performance, most of the students were conscientious and hard working. Some even participated in more than one paper. Most of the students needed to be reminded about the importance of staying on schedule. Only a few did not pull their own weight (in such cases, their grades and the team's performance was adversely affected).

To date only two reviews have not been completed. One was an attempt by a student who wished to work without team members. This is now discouraged. Nevertheless, the student made good progress, was graded accordingly, and the material is still topical and remains available for completion by a future class, in which case the student will be a co-author. The other incomplete involved a topic that preliminary work revealed to be too unwieldy and the team was advised to switch to a new topic, which was successfully completed. No submitted manuscript has not been eventually published. However, in a few cases a manuscript was rejected by the journal of first choice and was resubmitted to another journal. In this case, as in all cases, the students are kept apprised of the progress of the review process (which extends beyond the course duration) either by personal communication or by e-mail.

An unanticipated benefit of the elective course was that the information that was learned from the literature searches and manuscript preparation turned out to be useful for integration into the non-elective, compulsory courses of the PharmD programme. For example, information from almost

every manuscript was incorporated into the Pharmacology course. Hence, the benefits of the elective course extended beyond the registered elective students into the general student population.

The most negative aspect of such an elective is the lack of control over the journals' manuscript review process. In all cases, the unavoidable delay inherent in the review process extends acceptance of the submitted manuscript—and thus the students' positive feedback—well into the next semester, if not longer (some students received their reprints at the graduation ceremonies). In some cases, other vagaries encountered in the review process are frustrating to both the instructor and to the students. Since these can be anticipated but not avoided, the students are made aware of such possibilities early in the course.

In summary, in 1997 TUSP introduced an elective course to teach students about the processes involved in publishing a scientifically-rigorous review article and to provide them with the opportunity to prepare and submit such an article. We believe this is the first report of such a course. The result has been that 38 students, working in teams of 2–5 students each, have published 11 papers in peer-reviewed journals. Some students have co-authored more than one paper.

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APPENDIX A

(1) *The neuropharmacology of St. John's wort (Hypericum)*. (*Annals of Pharmacotherapy* **32**: 1201–1208, 1998). *Objective*: To review preclinical information related to possible antidepressant mechanism(s) of action of St. John's wort in order to address the issue of whether its purported clinical effectiveness has a rational pharmacologic basis. *Data sources*: Primary and review articles were identified by MEDLINE search for the period 1966 to January 1998, and through secondary sources. Many of the original German articles had English Abstracts, but where necessary German papers were translated into English. The results of a new screen of hypericin activity at receptor and uptake sites is summarized. *Study selection and data extractions*: All of the articles identified from the data sources were evaluated and all information deemed relevant was included in this review. *Data synthesis*: The neuropharmacology of St. John's wort has been examined in only a few studies. A mechanism similar to that of the synthetic antidepressants—e.g. the selective serotonin reuptake inhibitors (SSRIs) or monoamine oxidase inhibitors (MAOIs)—might play a role, but other mechanisms are possible. *Conclusions*: Hypericum extracts have only weak activity in assays related to mechanisms of the synthetic antidepressants—i.e. inhibition of MAO, COMT (catechol O-methyl transferase) or serotonin reuptake. It has been postulated that the clinical efficacy of St. John's wort could be attributable to the combined contribution of several mechanisms, each one too weak by itself to account for the overall effect. The recent demonstration of a significant affinity of hypericin for 5 receptors presents new possibilities for consideration.

(2) *Indirect modulation of dopamine D₂ receptors as potential pharmacotherapy for Schizophrenia: I. Adenosine agonists*. (*Annals of Pharmacotherapy* **33**: 480–488, 1999). *Objective*: To review preclinical and clinical information related to pharmacologic modulation of

dopamine D₂ receptors as potential novel antipsychotic therapy. Specifically, to summarize the data that suggests a modulatory action of adenosine A_{2A} receptors on dopamine D₂ receptors and, hence, a possible rational role of adenosine A_{2A} agonists as novel antipsychotic agents. *Data sources:* Primary and review articles were identified by MEDLINE search (for the period 1966 to May 1998) and through secondary sources. *Study selection and data extractions:* All of the articles identified from the data sources were evaluated and all information deemed relevant was included in this review. *Data synthesis:* For all of the older and many of the newer antipsychotic agents there is a strong correlation between clinical antipsychotic activity and affinity for dopamine D₂ receptors. Unfortunately, dopamine D₂ receptors are believed also to be involved in the adverse effect profile of these agents. The indirect modulation of dopamine D₂ receptors, rather than direct block, might produce antipsychotic effects without the usual adverse effects. Several lines of evidence from animal studies suggest that the use of selective A_{2A} agonists might represent a novel approach to the treatment of psychoses. *Conclusions:* Dopamine receptor modulation might represent a novel antipsychotic approach or adjunct therapy. The data regarding adenosine agonists (particularly selective A_{2A} receptor agonists) are inconclusive at the present time. Direct clinical demonstration of effectiveness is required.

(3) *Substance P antagonists: the next breakthrough in treating depression?* (*Journal of Clinical Pharmacy and Therapeutics* 24: 461–469, 1999). Several lines of evidence implicate the neuropeptide substance P in depression, either in the pathogenesis or as a novel target for amelioration of symptoms. NK1 (substance P) receptor antagonists have been reported to have antidepressant-like actions in animal models. The first clinical trial of an NK1 antagonist showed promising results. A second trial, using a more potent compound, is underway. If the clinical trials show that NK1 (substance P) antagonism represents a well-tolerated, distinct mechanism for antidepressant activity, novel antidepressant agents will emerge as mono- or adjunct-therapy.

(4) *Could a common biochemical mechanism underlie addictions?* (*Journal of Clinical Pharmacy and Therapeutics* 25: 11–20, 2000). The subject of "drug addiction" is multifaceted and many aspects of it (even some of the definitions) are controversial. Collateral medical problems include the spread of HIV and Hepatitis C virus secondary to i.v. drug abuse and effects on prenatal brain development. Progress in the understanding of the causes of addictions and its treatment has been impeded by the lack of a unifying biochemical theory. However, recent evidence suggests that some common mechanism might underlie addictions to otherwise

apparently unrelated drugs. A major hypothesis has emerged suggesting that the neurotransmitter dopamine (DA) might play a central role in the molecular mechanisms of at least some addictions. If so, it would represent an important target for discovery of effective pharmacotherapy and revolutionize the pharmacist's role in treating addictions. This short overview outlines the status of the theory of a common biochemical mechanism of drug addiction.

(5) *Lung opioid receptors: pharmacology and possible target for nebulized morphine in dyspnea* (*Life Sciences* 66: 2221–2231, 2000). Opioid receptors are located throughout the respiratory tract. Yet, these have received relatively scant attention compared to other opioid receptors. The most abundant sites within the respiratory tract appear localized within the alveolar walls, other sites appear to line the smooth muscle within the trachea and main bronchi near the lumen. There is about 100-times greater [³H]morphine binding density within the bronchioles and lobes than in the main bronchi or trachea. In addition to the usual μ , δ and κ types of opioid receptors, "non-conventional" opioid binding sites have been suggested, although the function of these or of the other opioid receptors in the pulmonary tract is not known. However, they might explain the otherwise counterintuitive apparent utility of morphine treatment of dyspnea. Dyspnea is a common and distressing symptom in terminally ill cancer patients and patients with chronic lung disease. It results from multiple causes, is difficult to treat and is a significant precipitating factor for late-stage hospital or hospice admissions. Nebulized morphine or other opioids have been reported to have beneficial effect, but the mechanism by which opioids might produce this seemingly contradictory effect is not clear. We review here lung opioid receptor distribution, pharmacology and possible clinical relevance in the treatment of dyspnea.

(6) *Indirect modulation of dopamine D₂ receptors as potential pharmacotherapy for Schizophrenia: II. Glutamate (ant)agonists.* (*Annals of Pharmacotherapy* 34: 788–797, 2000). *Objective:* To continue our overview of potential novel antipsychotic pharmacotherapy based on the indirect modulation of dopamine D₂ receptors or neurotransmitter functioning. Specifically, in this second article, to summarize the published preclinical and clinical data that suggests the possible use of glutamate receptor agonists or antagonists as novel antipsychotic agents. *Data sources:* Primary and review articles were identified by MEDLINE search (for the period 1966 to 1999) and through secondary sources. *Study selection and data extractions:* All of the articles identified from the data sources were evaluated and all information deemed relevant was included in this review. *Data synthesis:* The standard antipsychotic

drugs, whose clinical activity correlates with affinity for dopamine D₂ receptors, alleviate some of the positive symptoms of schizophrenia, but have only limited impact upon negative symptoms. Several lines of evidence implicate glutamate-receptor system dysfunction(s) in schizophrenia, either as causative or contributory factors. In addition, several standard antipsychotic drugs modulate glutamate or glutamate receptor activity, suggesting an alternative view of their mechanism of antipsychotic action. Preliminary studies have shown that drugs, which modulate glutamate brain levels, have positive effects in animal models of schizophrenia. *Conclusions:* A role for glutamate in the pathogenesis or pharmacotherapy of schizophrenia is suggested from anatomic (interactions between glutamatergic and dopaminergic systems in relevant brain regions), physiologic (implication of glutamate-receptor dysfunction) and pharmacologic (modulation of glutamate or glutamate receptors) evidence. Therefore, compounds which function at glutamate receptors might represent a novel approach to the treatment of the disease or to the amelioration of symptoms either as monotherapy or as adjunct to dopamine D₂ receptor antagonists.

(7) *Actions of Ginkgo Biloba related to potential utility for the treatment of conditions involving cerebral hypoxia.* (*Life Sciences* 67: 1389–1396, 2000). Neuronal hypoxia results from a variety of cerebrovascular accidents or "normal" age associated anatomic changes. The consequences vary from mild deficits in neurologic function to massive neuropathology. Present pharmacotherapeutic therapy is not ideal. Two apparently disparate approaches to the search for better treatment or prevention—one involving reassessment of herbal remedies as "alternative" medicine and the other one involving the desirability of increased structural diversity in HTS (high-throughput screening) libraries and as combinatorial chemistry templates—have converged in a rekindling of interest and a reevaluation of the pharmacologic properties of substances such as extract from the leaves of *Ginkgo biloba* Linne (form. *Salisburia adiantifolia* Sm.). There are reports of positive results from a small number of controlled clinical trials (albeit with small numbers of patients) sufficient to suggest that "Ginkgo" might have therapeutic benefit in some situations or subset of patients. The pharmacologic mechanism by which Ginkgo might be able to provide the observed effect is not clear. However, it is believed that the flavonoid and terpenoid components of Ginkgo extract might produce beneficial therapeutic effects through mechanisms acting separately or in concert, such as antagonism of PAF (platelet activating factor), antioxidant and metabolic actions, and effects on neurotransmitters. These mechanisms are reviewed in this article.

(8) *Is there a basis for novel pharmacotherapy of autism?* (*Life Sciences* 67: 1667–1682, 2000). No medication has yet been shown to consistently alter the symptoms or the course of autism in the majority of patients. The present pharmacotherapy is mainly palliative and sometimes effective in attenuating specific behaviors. The search for better treatment involves examination of the underlying pathophysiology, the genetic or environmental etiology (including possible iatrogenic causes), and assessment of the clinically generated evidence of efficacy, including serendipitous or unexplained findings. Subtle neuroanatomic and neurochemical changes are being explored and there are anecdotal reports or limited clinical trials that suggest some therapy might be possible. Secretin is a surprising recent addition to the list of candidates. The pharmacologic mechanism by which these agents might provide such effect is not clear, but hypotheses are beginning to emerge. In addition, the prevention of some uncertain number of autism cases is being investigated by examination of certain vaccinations as putative causative or contributory factors. These topics are reviewed in this article, which has the additional purpose of stimulating novel drug discovery efforts for this enigmatic disorder.

(9) *Insulin receptors and insulin action in the brain: review and clinical implications.* (*Neuroscience and Biobehavioral Reviews* 24: 855–872, 2000). Insulin receptors are known to be located on nerve cells in mammalian brain. The binding of insulin to dimerized receptors stimulates specialized transporter proteins that mediate the facilitated influx of glucose. However, neurons possess other mechanisms by which they obtain glucose, including transporters that are not insulin-dependent. Further, insulin receptors are unevenly distributed throughout the brain (with particularly high density in choroid plexus, olfactory bulb and regions of the striatum and cerebral cortex). Such factors imply that insulin, and insulin receptors, might have functions within the central nervous system in addition to those related to the supply of glucose. Indeed, invertebrate insulin-related peptides are synthesized in brain and serve as neurotransmitters or neuromodulators. The present review summarizes the structure, distribution and function of mammalian brain insulin receptors and the possible implications for central nervous system disorders. It is proposed that this is an under-studied subject of investigation.

(10) *Indirect modulation of dopamine D₂ receptors as potential pharmacotherapy for schizophrenia: III. Retinoids.* [*Journal of Clinical Pharmacy and Therapeutics* 27: 161–168, 2002]. Present antipsychotic drugs, whose clinical activity correlates with direct binding to dopamine D₂ or other receptors, alleviate some of the symptoms of schizophrenia, but not all

and not completely in many patients. In continuation of our overview of potential novel antipsychotic pharmacotherapy that would be based upon *indirect* modulation of dopamine or other neurotransmitter functioning, we focus in this article on the postulated use of retinoid analogs as novel antipsychotic agents. Several lines of evidence can be viewed as implicating retinoid dysregulation in schizophrenia, either as a causative or contributory factor. It has been proposed that using retinoid analogs to alter the downstream expression of dopamine D₂ receptors might represent a novel approach to the treatment of the disease or amelioration of symptoms when used either as monotherapy or as adjunct pharmacotherapy to dopamine D₂ receptor antagonists.

(11) *Potential novel targets for Alzheimer pharmacotherapy: I. Secretases.* [Journal of Clinical Pharmacy and Therapeutics 27: 169-184, 2002].

The prevailing major theory of Alzheimer disease (AD) is that insoluble amyloid β -peptide ($A\beta$) found in the cerebral plaques characteristic of the disease is causative or is at least a contributing factor. According to this theory, inhibition of aberrant $A\beta$ production should prevent or at least limit the extent of AD pathophysiology. Since three "secretase" enzymes (α , β , and γ) catalyze the proteolytic cleavage of APP (the precursor protein of $A\beta$), one or more secretases have become targets for potential novel AD pharmacotherapy. Secretase inhibitors have been designed and are in various stages of development. The clinical trials of these compounds will, if positive, result in drugs with dramatically better clinical efficacy or, if negative, will force a reassessment of the theory about the role of $A\beta$ in AD.