and has been evaluated in clinical studies in diverse patient populations demonstrating up to 80% efficacy compared with 25% of men taking a placebo, a finding that is statistically significant.[11] Efficacy is present regardless of patient age, the etiology of erectile dysfunction(ED) (psychogenic, organic, or mixed), or the baseline severity of the condition.[12] The efficacy of sidenafil encouraged increased numbers of patients with erectile dysfunction to face the problem with oral medication, a more-convenient, less-invasive method than any other previous treatment. It also stimulated much interest in the pharmaceutical industry for developing other effective oral medications. To the present, there are 3 drugs currently undergoing clinical trials:

1. IC351 (Cialis™, Lilly-ICOS)[13]

This is a novel phospho-diesterase-5 (PDE-5) inhibitor with an efficacy profile comparable to that of sidenafil but with a higher selectivity for PDE-5 and with essentially no visual side-effects. It is rapidly absorbed independent of meals, reaches a maximum plasma concentration at 2h, and has a mean half-life of 17.5h with low hepatic clearance, so the expected duration of pharmacologic action is about 24h. It is expected to obtain approval from the Food and Drug Administration (FDA) in the US in 2002.

2. Vardenafil (Nuviva™, Bayor)[14]

This is another PDE-5 inhibitor 4 to 5 times more potent than sildenafil with identical pharmacological reaction, efficacy, and safety profiles. The drug is effective 1h after ingestion with a half-life of about 8h. It is under registration in the US and EU, and more than 1000 patients have been administered vardenafil on demand at flexible doses of 5, 10, and 20 mg, the latter being the most well accepted.

3. Apomorphine (Uprima™ or Ixense™, Abott)[15]

Sublingual apomorphine has been approved in several European countries for the treatment of erectile dysfunction. Its main action is on the dopamine receptors in the central nervous system presumably in the hypothalamus. Erections occur rapidly within 10 to 25 min after sublingual administration only in the presence of sexual stimulation which indicates that the drug is not an aphrodisiac. The dosage is 2 to 4 mg, with a 55% success rate (vs 38% for a placebo) at 4 mg. The side effects include nausea (17%), dizziness (10%), and vomiting (3%). A 0.6% incidence of syncope was noted in clinical trials.

Gene Therapy for Erectile Dysfunction

The human penis is an ideal organ for gene therapy because of its external location and the fact that smooth muscle (cavernosal sinus) relaxation is the final step in penile erections. Many molecules and enzymes in the signal transduction pathway for smooth muscle relaxation can be potential targets for treatment of erectile dysfunction. Up to now, there are several groups of researchers who have successfully performed gene therapy in animal experiments with definite results. However, regulatory approval may not allow its use for the treatment of erectile dysfunction in the near future. The following reports are promising and may become preventive or therapeutic options for erectile dysfunction within the next decade:

1. The transfection of a nitric oxide gene into old rats penises was able to improve erection.[16]
2. Gene therapy with a potassium channel opener produced significantly improved erections in diabetic rats.[17]
3. Myoblast-mediated gene therapy was more successful in delivering iNOS into the rat penis than were direct viral or plasmid transfection methods.[18]
4. Gene therapy with eNOS significantly improved the erectile response in old rats.[19]
5. Endothelial cells were successfully transplantated into the corpus cavernosum, and this may be a more-efficient method of gene transfer.[20]
6. Systemic growth hormone can enhance regeneration of nitric oxide synthase-containing penile nerves after cavernous nerve neurotomy.[21]
7. The brain-derived neurotrophic factor (BDNF) gene mediated by an adeno-associated virus (AAV) can enhance the recovery of the cavernous nerve and erectile function in neurogenic ED rats.[22]